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Title: Barriers and determinants of asthma control in children and adolescents in Africa: A systematic review.

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ABSTRACT

Objective: To identify reasons for poor asthma control in African children and adolescents.

Design: Systematic review

Data sources: The PubMed, Scopus, CINHAL, PsycINFO, MEDLINE and Web of Science databases were systematically searched up to 31 May 2020. Hand searching was done on Sabinet, African Journal online and Google Scholar.

Eligibility Criteria: Studies identifying barriers to asthma control, where asthma control was assessed by the validated Asthma control test (c-ACT/ACT) and/or Asthma control questionnaire (ACQ) were included.

Data extraction and synthesis: Two reviewers independently selected studies for inclusion with disagreements resolved by a research team discussion, including a third reviewer. Data was extracted using the Cochrane Effective Practice and Organization of Care data collection form**.** The quality of the included studies was assessed using the modified Newcastle-Ottawa quality assessment scale. Identified barriers were reported in a thematic narrative synthesis.

Primary outcomes: Poorly controlled asthma and associated factors.

Results: From 914 records, three studies conducted between 2014 and 2019 in Nigeria, Uganda and South Africa met the inclusion criteria. A total of 883 children aged 4 - 19 years were analysed. Older age, concurrent allergy and city-dwelling significantly impacted asthma control. Pooled uncontrolled asthma prevalence was 39,8%. Few children with asthma symptoms in the community had ever used inhaled

corticosteroids (6,7%), and identified reasons included lack of asthma diagnosis (38,8%) and no prescribed treatment (47,6%).

Conclusion: Asthma control in African children is impacted by age, allergy, urbanisation and lack of access to asthma diagnosis and treatment. **PROSPERO (registration no. CRD42020196755)**

KEYWORDS: urbanization, access to care, community-based research, asthma outcomes, public health, air quality, low-and-middle-income countries

Strength and limitations

- Only the sufficiently validated ACT/cACT was used to assess asthma outcomes.
- Limited evidence was available and 3 studies were identified.
- The heterogeneity of the studies precluded a meta-analysis.
- Factors reported within emerging themes, were additional to and matched those classified in current literature.

INTRODUCTION

Asthma is a chronic non-communicable respiratory disease affecting over 340 million people worldwide, the majority of whom reside in low-and-middle-income countries (LMICs). [1] Countries with the highest childhood asthma prevalence in Africa, South Africa (20.7%), Congo (19.9%), and Ivory Coast (19.3 %), [2] are also regions with increasing urbanisation rates. [3] Factors including poor air quality and lack of access to health facilities may be driving the rising asthma rate and impacting asthma control.

[4] However, in this setting, asthma research and research infrastructure remain lacking. [5-8]

The most commonly used validated tools for asthma control assessment are the composite score instruments; Asthma Control Test (ACT), Child Asthma Control Test (cACT) and the Asthma Control Questionnaire (ACQ). [9] The ACT and ACQ provide a quantitative assessment of asthma control and have been designated as core measures by the National Institutes of Health (NIH) for clinical research and observational studies.[10] [11] ACT and ACQ are simple methods that can help quantify the impact of barriers on asthma control, [12] which may not be comparable between high-income countries (HICs) and LMICs. [13] This review was conducted to collate data on reported barriers to asthma control in children and adolescents in Africa.

METHODS

The systematic review is registered with PROSPERO (registration no. CRD42020196755). We used the PECO acronym to aid with the systematic search. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) reporting standards were followed. [14]

Search strategy

The following databases were searched: PubMed, Scopus, CINHAL, PsycINFO, MEDLINE and Web of Science. The search methodology for all the databases is provided in the supplementary material (Table S1). Hand searching of the following databases was also conducted: Sabinet, African Journal online and Google Scholar. Only scientific articles written in English with date restrictions from 01 January 2000 to 31 May 2020 were included.

The search strategy was structured to include terms for "Child", “Asthma”, "Barriers", "Asthma Control Test", "Africa" and or variations of these.

Selection of studies

Studies identified from searching electronic databases were combined and duplicates removed. References were independently screened by two reviewers (REM, OK) using a 3-stage review of title and abstract, followed by a full-text review of included studies. The full text of potentially eligible studies was screened against the review criteria and potential articles identified. At each stage, disagreements were resolved by a team discussion with a third reviewer (RM).

Inclusion and exclusion criteria

The study's focus was to identify barriers associated with poor asthma control in African children and adolescents with doctor-diagnosed/suspected asthma, where the validated ACT/cACT or ACQ tool was used to assess asthma control. The population included children between the ages of 6 -18 years. Studies were included with broader age ranges if children aged 6 -18 years were reported separately, or if >50% of the population were children within this age range.

Studies published from January 2000 to May 2020 were included to ensure the encompassing of all data since validation of the ACT and ACQ. Clinical trials assessing pharmaceutical treatment and diagnostic accuracy of tools were excluded. Grey literature from experts in the field, conference abstracts or unpublished material was also excluded. (Table 1.)

Table 1. Criteria for the search and rules devised to facilitate inclusion/exclusion criteria

Search strategy	Definition	Rules
Population	Children and adolescents between age 6 -18 years with a doctor diagnosis or a baseline prescription for asthma treatment or presumed diagnosis of asthma based on a history of recurrent wheeze.	*Included* Studies with broader ranges of ages if children age 6-18 were reported separately or if >50% of the population were children within this age range. Excluded Studies in adults (>18years)
Exposure	Environmental related factors Pollution (indoor and outdoor), environmental tobacco smoke, mould, biomass fuels, pets, physical exercise, sedentary lifestyle, antibiotic use, paracetamol use, industrial combustion, respiratory infections. Patient-related factors Attitudes, knowledge and perceptions, adherence, beliefs, inhaler technique, lifestyle, relationships, communication Healthcare and doctor related factors Availability of treatment and healthcare facilities, doctor asthma knowledge, time spent on asthma education, availability of medications. Comorbidities Allergic Rhinitis, Obesity, Obstructive Sleep Apnoea (OSA) Gastroesophageal Reflux Disease (GERD)	*Included* Studies aiming to identify exposures that had a quantifiable impact on asthma control. *Excluded:* • Clinical trials assessing pharmaceutical treatments. • Studies assessing the diagnostic accuracy of tools. • Studies assessing the validity of tools.

Comparison (if applicable):	Usual care in people of the same age with well-controlled asthma	
Outcome	Asthma control measured using ACT /cACT and/or ACQ	*Excluded* Studies using tools for measuring asthma control other than ACT/cACT and/or ACQ
Timeframe	20 years between January 2000 – May 2020	*Excluded* Studies conducted before January 2000 and after May 2020
Setting	Africa	*Excluded* Studies not done in Africa
Study	Cohort, case-control, cross-sectional	*Included* Studies identifying exposures that impact asthma control as measured by cACT/ ACT and/or ACQ

ACT: asthma control test; cACT: child asthma control test; ACQ: asthma control questionnaire

Data extraction

The full texts of all studies found to be relevant and meeting the inclusion criteria were retained for data extraction and final synthesis. Data including study design, setting, population, authorship and statistical analysis was extracted using a standardised data extraction form modified from the Cochrane Effective Practice and Organization of Care data collection form.[15] The authors were contacted where clarification was required and data was missing. The selection process was summarised using a PRISMA flow diagram (Figure 1).

Quality assessment

The included studies' quality was assessed using the modified Newcastle-Ottawa Scale for cohort, case studies, and cross-sectional studies. [16] (Table S2).

Data analysis and synthesis

We anticipated that the population and statistical analysis heterogeneity of the studies would preclude a formal meta-analysis. We therefore grouped into themes asthma control barriers corresponding to literature; patient, environmental, healthcare/doctor-related factors and comorbidities[12 13]. (Table S3). As asthma control was assessed using the same tool, we calculated the pooled prevalence of asthma control using a random-effects model to calculate a weighted summary. Statistical analyses were performed using MedCalc-Software, Ostend, Belgium; http://www.medcalc.org; 2018.[17]

Patient and public involvement

The results of the study were used to inform community engagement and asthma education workshops at schools where the authors are steering asthma education and other asthma-related research.

RESULTS

Search Results

There were 914 articles identified: 863 articles through electronic database searching (EBSCO host = 27, PubMed = 136, Web of Science = 97, Scopus = 603) and an additional 51 articles through hand searching (Google scholar = 23, Sabinet = 12, AJOL = 16). The total number of articles found after duplicates were removed was 498. Of the 498 articles screened, 484 were excluded as they were not appropriate or did not relate to the study. The remaining 14 full articles were assessed for eligibility, and 11 articles were excluded for the following reasons: wrong age group =2, Did not use ACT/ACQ = 2, not original research = 2, assesses impact rather than barriers of poor asthma control = 5. Three studies met the inclusion criteria. (Figure 1.)

[INSERT FIGURE 1 HERE]

Characteristics of the studies

All three studies conducted in Nigeria, South Africa and Uganda [18-20] were cross-sectional; two hospital-based and one community-based. The sample size was smaller for hospital-based studies with 207 and 115 participants in Nigeria[18] and South Africa[19], respectively, compared to the community-based study of 561 participants in Uganda. [20] Publication dates ranged from 2014 to 2019. The ages of participants ranged from 4 - 19 years. Asthma diagnosis was based on doctor diagnosis [18 19] guided by the Global Initiative on Asthma (GINA),[18] and symptom screening by the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. [20] One study adjusted for age, gender and concurrent allergy [20], while the rest did not report adjusting for potential confounders, reducing their quality score. [18 19] (Table 2. and Table S2)

Table 2. Characteristics of included studies

Author ref	Study type	Setting	Year of Publication	Country of origin	Sample Size	Age ranges (years)	Asthma definition	Asthma control definition	Recruitment	Exposures	Quality Score	Reviewers comment
Ayuk et al. (20)	Cross sectional	Hospital	2018	Nigeria	207	4-18	Doctor Diagnosis, GINA	ACT / cACT >19 controlled <19 uncontrolled	Consecutive enrolment for 1 year from a group of children attending the asthma clinic	Family size, socioeconomic status, urban vs rural dwelling, allergy status (by ISAAC), Triggers (particulate and non-particulate)	7/10	Author contacted for further information on participant numbers.
Garba et al. (21)	Cross sectional	Hospital	2014	South Africa	115	5-18	Doctor diagnosis	ACT / cACT = 25 (ACT)/ 27 (cACT) total control >19 well-controlled ≤ 19 uncontrolled 16-19 somewhat controlled <16 Poorly controlled	Consecutive enrolment for 4 months from a group of children attending the asthma clinic	Presence of a smoker at home, presence of pets, cockroaches and use of biomass fuel, the child's sleeping environment (dust, carpets and soft toys in the bedroom). Compliance with medications and inhaler technique. Allergy status (by clinical examination)	5/10	Author contacted for further information on recruitment strategy, data analysis and participant numbers.
Mpairwe et al. (22)	Cross-sectional	Community School	2019	Uganda	561	5-17	Screening ISAAC questionnaire	ACT / cACT > 19 Well controlled 15-19 partly controlled <15 Poorly controlled	Recruitment from children with self-reported breathing problems at schools in an urban area	Age, sex, regular physical exercise as recommended by WHO, area of residence in 1st 5 years of life (rural, town or city), concurrent allergy, antimalarials	10/10	Describes participants as derived from a large case-control [21] study to investigate risk factors of asthma

WHO: world health organisation; ACT: asthma control test; cACT: child asthma control test; ISAAC: international survey on asthma and atopy in children; GINA: global initiative for asthma

21. Mpairwe H et al. Risk factors for asthma among schoolchildren who participated in a case-control study in urban Uganda. Elife. 2019;8:e49496.

Assessment of asthma control

All the studies measured asthma control using ACT and cACT. Scores were based on the cutoff point of >19 for controlled asthma and ≤ 19 for uncontrolled asthma. The prevalence of poor asthma control in the participants using pooled data for the clinic-based population and the community-based population was 35.7% and 44.5%, respectively. The pooled prevalence of uncontrolled asthma for the whole population was 39.8% with considerable heterogeneity, I^2 = 84% p=0.002. (Figure 2)

[INSERT FIGURE 2 HERE]

Thematic synthesis

Patient-related factors

Age

Two studies assessed the impact of age on asthma control. The large community-based study showed that older age (13 -17 years) was significantly associated with poorer asthma control (-1.07 [-1.20, -0.94], p < 0.0001). [20] The exception was a small clinic cohort of moderate quality, which showed no association. [19]

Gender

Two of the studies [19 20] that examined gender showed no significant association with asthma control.

Asthma medication use

Two studies [19 20] examined the use and compliance of asthma medication. The study amongst school-going children [20] showed that the majority (73%) had never used inhaled asthma medications. Additionally, regular use of inhaled asthma medication in

the last 12 months was inadequate for salbutamol (18.1%) and corticosteroid (6.7%) even though the majority (55.8%) had a doctor diagnosis of asthma. Although not significant, in the same cohort, children with poorly controlled asthma preferred regular use of (salbutamol and prednisone) tablets rather than inhaled salbutamol and corticosteroids. [20] Conversely, in the cohort of children attending asthma clinic [19], good adherence to medications was seen in 82.6% of patients. In these doctor-diagnosed children, asthma control was significantly associated with good adherence to medication, where 37.9% and 62.1% of patients had uncontrolled asthma and controlled asthma, respectively (x^2=0.217, p=0.002). [19]

Ethnicity

There was no significant association between asthma control and ethnicity (x^2=3.22, p =0.359) in Black-African, Caucasian, Mixed-ethnicity and Indian participants in South Africa[19].

Environmental related factors

Two studies conducted in Uganda[20] and Nigeria[18] examined the effects of rural vs urban domicile on asthma control. The school-based Ugandan cohort showed that city residence in early life was associated with poor asthma control (-1.99[-3.69, -0.29], p =0.02). [20] In contrast the clinic-based cohort in Nigeria showed, although without significance, that within the rural community, more children with current allergies had better control of their asthma (85.7%) when compared to their urban counterparts (66.7%). Interestingly, the children who lived in rural areas *without* concurrent allergy had poorly controlled asthma (50.0%) compared to their urban counterparts (28.3%), Fisher's exact test =2.076, p= 0.17, although this too was not significant. [18]

All three included studies considered the presence of asthma triggers in their participants' environments, but only the South African study examined these triggers in relation to asthma control. Common triggers included dust, cold air, physical exercise, fumes or air pollution, pollen, pets, smoking and biomass fuels. (Figure 3.) In the South African cohort, home circumstances including dust, cockroach, carpet, pets, toys in bed, and smoking were not found to be associated with asthma control. [19] The use of biomass fuel was uncommon in South Africa (6.1%) compared to Nigeria (22.1%) and was not found to be significantly associated with asthma control (x^2 =6.202, p =0.185). [18 19]

[INSERT FIGURE 3 HERE]

Healthcare and doctor related factors

Only the field-based study in Uganda, reported the impact of healthcare-seeking behaviour on asthma control. In 553 children who reported treating their asthma in the last year, 26.8% reported having ever used inhaled asthma medications, and a similar proportion, 29.7%, reported having ever used herbal remedies for asthma management. On enquiry about previous asthma assessments and follow-up, 73 (13.2 %) visited a health facility to monitor their asthma, 45 (8.2%) children had ever had a lung function test; two (0.4%) had ever used a peak flow meter as an asthma monitoring tool at home, and only three (0.5%) had a personal written asthma action plan. [20] The reason for having never used inhaled asthma medication was investigated in 405 children and included: inhaled asthma medications had never been prescribed for them (47.6%), never been diagnosed (38.8%), high cost of inhalers (4.5%), fear of side effects of inhalers (4.5%), alternative treatment with salbutamol or steroid tablets (1.4%) and non-medicinal treatment, i.e. wrapping up in warm clothes and resting. [20]

Comorbidities

All three studies assessed children for allergic rhinitis, but only two [18 20] in relation to asthma control. In the larger powered community-based study, [20] children with concurrent allergic rhinitis were more likely to have lower asthma control scores (-1.33 [-2.28, -0.38], p=0.006), whereas no significant association was found between atopy and asthma control in the small cohort clinic-based study. [18] However, in the latter study, children with current allergy had more emergency hospital visits due to asthma exacerbations (x2 = 10.09 [df 1] p = 0.002; Spearman's R =0.22, p = 0.001). [18]

DISCUSSION

Older age, concurrent allergic rhinitis and early life urban residence are barriers similar to HICs and significantly impact asthma control in African children. Access to healthcare and appropriate asthma medication remains limited, with a minority of children with asthma symptoms ever having used ICS.

Older age

Mpairwe et al. found adolescents in Uganda have inadequate asthma control and outcomes. Similarly, the age group 12 -17 years was more predictive of exacerbations than other age groups in a European cohort study using the General Practice Research Database (GPRD) [22]. One reason for this can be explained by adolescent studies that show poor adherence compared to other age groups. [23] Social stigma, forgetfulness and poor understanding of medication play a significant role in adherence and warrant further exploration. [24 25]

Concurrent allergic rhinitis

The Ugandan and Nigerian studies found that children with AR had less well-controlled asthma and were more likely to be hospitalised. Similarly, in a large UK retrospective cohort of 9522 children with asthma, the presence of AR significantly increased the likelihood of physician visits and more than doubled the likelihood of hospitalisation. Furthermore, drug use and costs were significantly higher among children with asthma and concurrent AR. [26] Active search and recognition of AR when assessing children remains critical in comprehensive asthma management.

Rural versus urban residence

Studies in Africa show a decreasing gradient in asthma prevalence between urban and rural areas [27 28]. In this context, biomass fuel exposure remains a significant contributor to inflammatory lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). [29 30] Few studies in Africa have compared asthma control between rural and urban areas. [18 20 31 32] Urban residence was significantly associated with poorly controlled asthma in Uganda, where asthma risk among schoolchildren [20] was three times higher in children who in early life resided in cities rather than rural areas. [21] Similarly, rural to urban migration appears to be an important determinant of the increasing prevalence of wheeze among school-going children in Latin American cities. [33 34] Increasing asthma rates in peri-urban settings could be related to over-crowding, reduction of exercise, poorer air quality and changes in lifestyle and diets.

Access to diagnosis and health care

Six out of 10 children attending healthcare institutions have good asthma control, while a similar number of undiagnosed children in the community have poorly controlled asthma. [18-20] Even after a diagnosis of asthma, ICS use is limited in communities [20 35]

compared to clinic patients [19] who once diagnosed, have significantly better asthma control. The preference of tablets (salbutamol and corticosteroids) over ICS may largely be explained by their quick relief and ease of administration combined with underlying suboptimal knowledge and asthma medications cost. [35] Furthermore, traditional healers remain integral to medical care in communities due to local cultural practices and beliefs. There is a need to communicate asthma management strategies to communities in a culturally sensitive manner. [31 36] Triggers including dust, air pollution, pollen, pets, and smoking common across the globe, indicate the feasibility of a global checklist and the necessity of avoidance education. [37]

Strengths and limitations

We may not have identified all significant barriers that impact asthma control as other asthma control tools, i.e. Global Initiative for Asthma (GINA) and National Asthma Education Programme (NAEP), were excluded because they are not as sufficiently validated as the ACT and ACQ.[10] Nevertheless, we identified variables in each group classification for poor asthma control.[13] Our wide-ranging search strategy found no non-English articles requiring exclusion. The studies' heterogeneity in terms of outcome analysis and population precluded a meta-analysis; therefore, we reported all the factors within the emerging themes.

Implications for clinical practice, healthcare systems and policymakers

Strategies that improve medication access, including initiatives like the WHO Essential Medicines List, low-cost equipment like plastic spacers [38] and implementing culturally appropriate educational programs for healthcare workers and the public, remain vital. [39 40]

Implications for future research

Studies beyond healthcare institutions that include communities in identifying barriers and their impact on asthma control are needed in African children.

CONCLUSION

Asthma control barriers requiring focus in Africa are; lack of accurate diagnosis, limited access to inhaled therapy, lack of asthma knowledge and poor air quality. Better education and advocacy through community-based public interventions are needed to improve African children's asthma control and outcomes.

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Contributing Authors: REM, OM, RM designed the study and the search strategy. REM performed the literature search. REM, OM and RM performed the screening. REM performed the data extraction and analysis. REM, OM and RM interpreted the results. REM wrote the manuscript. All authors reviewed and approved the final version of the manuscript.

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Figure 1. Study eligibility chart according to PRISMA criteria

Figure 2. The pooled prevalence of poor asthma control in African children and adolescents, showing the proportion of uncontrolled asthma measured by the asthma control test (ACT) or child asthma control test (cACT).

Figure 3. Prevalence of asthma triggers among study participants across African studies using the ACT to identify asthma control barriers. ETS = environmental tobacco smoke. ACT = asthma control test

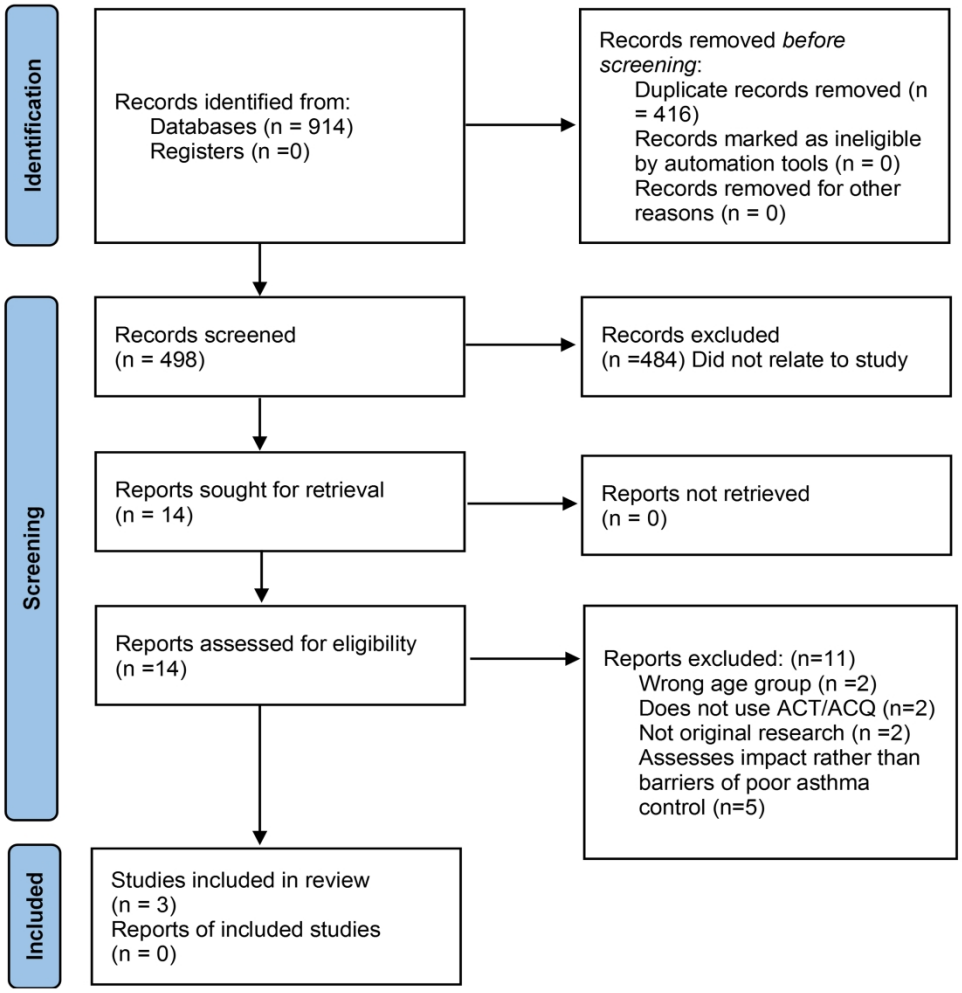

Figure 1. Study eligibility chart according to PRISMA criteria

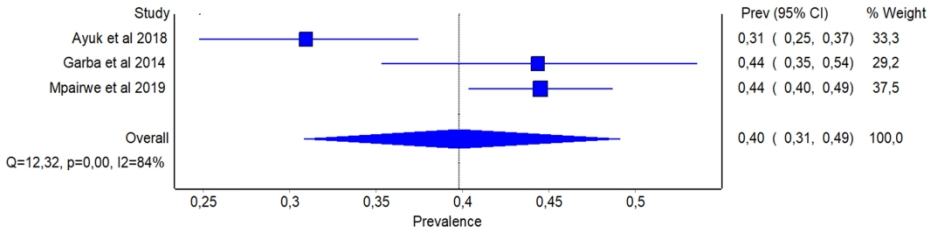

Figure 2. The pooled prevalence of poor asthma control in African children and adolescents, showing the proportion of uncontrolled asthma measured by the asthma control test (ACT) or child asthma control test (cACT).

338x190mm (300 x 300 DPI)

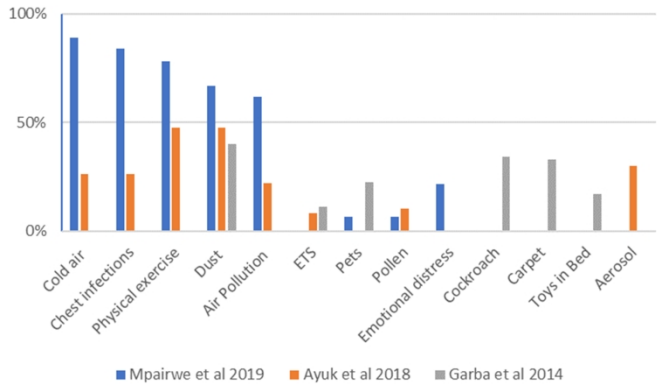

Figure 3. Prevalence of asthma triggers among study participants across African studies using the ACT to identify asthma control barriers. ETS = environmental tobacco smoke. ACT = asthma control test

338x190mm (300 x 300 DPI)

Table S1 SEARCH STRINGS Asthma control barriers in African children.

PUBMED SEARCH STRING

pediatric* or paediatric* or child* or kindergarten* or kindergarden* or "elementary school*" or schoolchild* or boy or boys or girl* or "middle school*" or pubescen* or juvenile* or teen* or youth* or "high school*" or adolesc* or pre-pubesc* or prepubesc*) OR (child* or adolesc* or pediat* or paediat* [Journal]) OR child[MeSH Terms] OR infant[MeSH Terms] OR adolescent[MeSH Terms] OR pediatrics[MeSH Terms] OR minors[MeSH Terms]
AND
Asthma control test OR Asthma control questionnaire OR ACT OR ACQ OR asthma control surveys OR asthma control assessment tool OR ACQ composite score OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
AND
Challenges OR Challenge OR Problem OR Problems barriers or Difficulties or Issues or Limitations or Obstacles OR predisposing factors OR enabling factors OR factors or precipitating factors OR reinforcing factors OR risk factors OR predictor or contributing factors or key factors or cause or correlation OR Factor, Risk OR Factors, Risk OR Risk Factor OR Population at Risk OR Risk, Population at OR Populations at Risk OR Risk, Populations at OR Causalities OR Multifactorial Causality OR Causalities, Multifactorial OR Causality, Multifactorial OR Multifactorial Causalities OR Multiple Causation OR Causation, Multiple OR Causations, Multiple OR Multiple Causations OR Reinforcing Factors OR Factor, Reinforcing OR Factors, Reinforcing OR Reinforcing Factor OR Causation OR Causations OR Enabling Factors OR Enabling Factor OR Factor, Enabling OR Factors, Enabling OR Predisposing Factors OR Factor, Predisposing OR Factors, Predisposing OR Predisposing Factor
AND
"asthma"[MeSH Terms] OR asthma[Text Word]OR Wheeze [All Fields])))))) AND ((((("africa"[MeSH Terms] OR "africa"[All Fields]) OR ("africa south of the sahara"[MeSH Terms] OR ("africa"[All Fields] AND "south"[All Fields] AND "sahara"[All Fields]) OR "africa south of the sahara"[All Fields] OR ("sub"[All Fields] AND "saharan"[All Fields] AND "africa"[All Fields]) OR "sub saharan africa"[All Fields]) OR ("angola"[MeSH Terms] OR "angola"[All Fields]) OR ("benin"[MeSH Terms] OR "benin"[All Fields]) OR ("botswana"[MeSH Terms] OR "botswana"[All Fields]) OR ("burkina faso"[MeSH Terms] OR ("burkina"[All Fields] AND "faso"[All Fields]) OR "burkina faso"[All Fields]) OR ("burundi"[MeSH Terms] OR "burundi"[All Fields]) OR ("cape verde"[MeSH Terms] OR ("cape"[All Fields] AND "verde"[All Fields]) OR "cape verde"[All Fields] OR ("cabo"[All Fields] AND "verde"[All Fields]) OR "cabo verde"[All Fields]) OR ("cameroon"[MeSH Terms] OR "cameroon"[All Fields]) OR ("central african republic"[MeSH Terms] OR ("central"[All Fields] AND "african"[All Fields] AND "republic"[All Fields]) OR "central african republic"[All Fields]) OR ("chad"[MeSH Terms] OR "chad"[All Fields]) OR ("comoros"[MeSH Terms] OR "comoros"[All Fields]) OR ("congo"[MeSH Terms] OR "congo"[All Fields]) OR ("cote d'ivoire"[MeSH Terms] OR ("cote"[All Fields] AND "d'ivoire"[All Fields]) OR "cote d'ivoire"[All Fields]) OR ("democratic republic of the congo"[MeSH Terms] OR ("democratic"[All Fields] AND "republic"[All Fields] AND "congo"[All Fields]) OR "democratic republic of the congo"[All Fields]) OR ("djibouti"[MeSH Terms] OR "djibouti"[All Fields]) OR ("egypt"[MeSH Terms] OR "egypt"[All Fields]) OR ("equatorial guinea"[MeSH Terms] OR ("equatorial"[All Fields] AND "guinea"[All Fields]) OR "equatorial guinea"[All Fields]) OR ("eritrea"[MeSH Terms] OR "eritrea"[All Fields]) OR ("ethiopia"[MeSH Terms] OR "ethiopia"[All Fields]) OR ("gabon"[MeSH Terms] OR "gabon"[All Fields]) OR ("gambia"[MeSH Terms] OR "gambia"[All Fields]) OR ("ghana"[MeSH Terms] OR "ghana"[All Fields]) OR ("guinea"[MeSH Terms] OR "guinea"[All Fields]) OR ("guinea-bissau"[MeSH Terms] OR "guinea-bissau"[All Fields] OR ("guinea"[All Fields] AND "bissau"[All Fields]) OR "guinea bissau"[All Fields]) OR ("kenya"[MeSH Terms] OR "kenya"[All Fields]) OR ("lesotho"[MeSH Terms] OR "lesotho"[All Fields]) OR ("liberia"[MeSH Terms] OR "liberia"[All Fields]) OR ("libya"[MeSH Terms]

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SCOPUS SEARCH STRING

pediatric* OR paediatric* OR child* OR kindergarten* OR kindergarden* OR "elementary school*" OR schoolchild* OR boy OR boys OR girl* OR "middle school*" OR pubescen* OR juvenile* OR teen* OR youth* OR "high school*" OR adolesc* OR pre-pubesc* OR prepubesc* OR child* OR adolesc* OR pediat* OR paediat* OR child OR adolescent OR pediatric* OR minor*
AND
"Asthma*" OR "Bronchial Asthma" OR "Bronchial" AND "Asthma" OR "Bronchial Asthma, Exercise Induced" OR "Exercise Induced Bronchial Asthma*" OR "Asthma*, Exercise-Induced" OR "Exercise Induced Asthma" OR "Exercise-Induced Asthma*" OR "Bronchospasm, Exercise-Induced" OR "Bronchospasm*, Exercise Induced" OR "Exercise-Induced Bronchospasm*" OR "Exercise Induced Bronchospasm" OR "Bronchial Spasm*" OR "Spasm*, Bronchial" OR "Bronchospasm*" OR "Wheez*" OR "Status Asthmaticus" OR "Bronchial Hyperreactivit*" OR "Respiratory Hypersensitivit*" OR "Bronchoconstrict*"
AND
"Asthma control test" OR "Asthma control questionnaire" OR ACT OR "Childhood asthma control test" OR C-ACT OR ACQ OR "asthma control survey*" OR "asthma control assessment tool" OR "ACQ composite score" OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
AND
Challenge* OR Problem* OR Barriers OR Difficult* OR Issue* or Limitation* OR Obstacle* OR "predisposing factor*" OR "enabling factor*" OR factors OR "precipitating factor*" OR "reinforcing factor*" OR "risk factor*" OR predictor OR "contributing factor*" OR "key factor*" OR caus* OR correlation* OR "Factor, Risk" OR "Factors, Risk" OR "Risk Factor" OR "Population at Risk" OR "Risk, Population" at OR "Populations at Risk" OR "Risk, Populations at" OR Causalities OR "Multifactorial Causality" OR "Causalities, Multifactorial" OR "Causality, Multifactorial" OR "Multifactorial Causalities" OR "Multiple Causation" OR "Causation, Multiple" OR "Causations, Multiple" OR "Multiple Causations" OR "Reinforcing Factors" OR "Factor, Reinforcing" OR" Factors, Reinforcing" OR "Reinforcing Factor" OR Causation* OR "Enabling Factor*" OR "Enabling Factor" OR "Factor, Enabling" OR "Factor*, Enabling" OR "Predisposing Factor*" OR "Factor, Predisposing" OR" Factor*, Predisposing"
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"africa" OR "africa" OR "africa south of the sahara" OR "Africa AND south" AND "sahara" OR "africa south of the sahara" OR "sub AND saharan AND africa" OR "sub Saharan africa" OR "angola" OR "angola" OR "benin" OR "benin" OR "botswana" OR "botswana" OR "burkinafaso" OR "burkina AND faso" OR "burkinafaso" OR "burundi" OR "burundi" OR "cape verde" OR "cape AND verde" OR "cape verde" OR "cabo AND verde" OR "caboverde" OR "cameroon" OR "central african republic" OR "central AND african AND republic" OR "central african republic" OR "chad" OR "comoros" OR "congo" OR "cote d'ivoire" OR "cote AND d'ivoire" OR "democratic republic of the congo" OR "democratic AND republic AND congo" OR "democratic republic of the congo" OR "djibouti" OR "egypt" OR "equatorial guinea" OR "equatorial AND guinea" OR "eritrea" OR "ethiopia" OR "gabon" OR "gambia" OR "ghana" OR "guinea" OR "guinea-bissau" OR "guinea AND bissau" OR "guinea bissau" OR "kenya" OR "lesotho" OR "liberia" OR "libya" OR "madagascar" OR "malawi" OR "mali" OR "mauritania" OR "mauritius" OR "comoros" OR "mayotte" OR "morocco" OR "mozambique" OR "namibia" OR "niger" OR "nigeria" OR "reunion" OR "rwanda" OR "atlantic islands" OR "atlantic AND islands" OR "saint AND helena" OR "saint helena" OR "sao AND tome AND principe" OR "sao tome and principe" OR "senegal" OR "seychelles" OR "sierra leone" OR "sierra AND leone" OR "somalia" OR "south africa" OR "south AND africa" OR "south sudan" OR "south AND sudan" OR "Swaziland" OR "tanzania" OR "togo" OR "tunisia" OR "uganda" OR "zambia" OR "zimbabwe"

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AND
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AND
Asthma control test OR Asthma control questionnaire OR ACT OR Childhood asthma control test OR C-ACT OR ACQ OR asthma control surveys OR asthma control assessment tool OR ACQ composite score OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
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EBSCO host: CINAHL Complete, Academic Search Complete, APA PsycInfo, CINAHL with Full Text, MEDLINE Complete, MEDLINE with Full Text) SEARCH STRING

((pediatric* or paediatric* or child* or kindergarten* or kindergarden* or "elementary school*" or schoolchild* or boy or boys or girl* or "middle school*" or pubescen* or juvenile* or teen* or youth* or "high school*" or adolesc* or pre-pubesc* or prepubesc*) OR (child* or adolesc* or pediat* or paediat* [Journal]) OR child[MeSH Terms] OR infant[MeSH Terms] OR adolescent[MeSH Terms] OR pediatrics[MeSH Terms] OR minors[MeSH Terms])) Search modes - Boolean/Phrase
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(environmental factors OR environmental influences OR environmental exposure) OR (environmental factors.mp. OR environmental influences.mp OR environmental exposure.mp. OR environmental tobacco smoke.mp. OR maternal smoking.mp. OR parental smoking.mp. OR Nitrogen Dioxide/ OR gas fire*.mp. OR cooker*.mp. mp. OR Volatile Organic Compounds/ OR cleaning agents.mp. OR chemicals.mp. OR glue*.mp. OR floor covering*.mp. OR dry cleaning.mp. OR Chlorine/ oR swimming pool*.mp. resin*.mp. OR varnish.mp. OR Paint/ OR ethyl benzene.mp. OR air fresheners.mp. OR toluene.mp. OR caulk*.mp. / OR Vehicle Emissions/ae, pc, to [Adverse Effects, Prevention & Control, Toxicity] OR plastic$.mp. OR phthalate$.mp. OR flame retardant$.mp. OR plasticizer$.mp. OR plasticiz$ polyvinyl chloride.mp. OR floor covering$.mp. OR adhesive$.mp. OR synthetic leather.mp. OR toy$.mp. OR cosmetic$.mp. OR indoor dust.mp. OR di 2-ethylhexyl phthalate.mp. OR pvc.mp. outdoor source$.mp. OR ozone.mp. OR sulphur dioxide.mp. OR traffic.mp. OR exhaust.mp OR coal fire$.mp. OR diesel.mp. OR weather.mp OR particulate matter.mp. OR UFP$.mp. OR transport.mp. OR industrial incineration.mp. OR firework$.mp. OR bonfire.mp. OR solid fuel.mp. OR heating$.mp. OR cooking.mp OR candle$.mp. OR vacuum$.mp. OR hoover$.mp. OR resuspension.mp. OR ingression.mp. OR incineration.mp. OR NOX.mp. OR mp. OR carpet*.mp. OR tetraethyl lead.mp. OR cerium oxide*.mp. OR cold air.mp. OR meteorolog*.mp. OR. temperature.mp. OR climate.mp. OR air pollut*.mp. OR total suspended particulate*.mp. OR coal.mp.OR wood.mp. OR peat.mp. OR biomass.mp. OR oil.mp. OR diacetyl.mp. OR allergens.mp. OR aspergillus.mp. OR cladosporium.mp. OR dust mite*.mp. OR cat*.mp. OR dog*.mp. OR horse*.mp. OR animal*.mp. OR pet*.mp. OR mould.mp. OR mold.mp. OR alternaria.mp.OR cockroach*.mp. OR mice.mp. OR rats.mp. OR pollen.mp. OR grass.mp. OR aeroallergen*.mp. OR IgE.mp. OR fungal spore*.mp. OR food allerg*.mp. OR glucan*.mp. OR peanut*.mp. OR egg.mp. OR milk.mp. OR dairy.mp. OR exercise.mp. OR 197. lipopolysaccharide.mp. OR endotoxin.mp. OR. respiratory syncitial virus.mp. OR rhinovirus.mp. OR influenza virus.mp. OR corona virus.mp. OR diet.mp. OR sulphite*.mp. OR sulfite*.mp. OR sodium metabisul*.mp. OR monosodium glutamate.mp. OR MSG.mp. OR sodium benzoate.mp. OR vitamin D.mp. OR vitamin E.mp. OR antioxidant*.mp. OR lipid*.mp. OR. drug*.mp. OR aspirin.mp. OR paracetamol.mp. OR antibiotic*.mp. OR NSAID*.mp. ORobesity.mp.) OR (Challenges OR Challenge OR Problem OR Problems barriers or Difficulties or Issues or Limitations or Obstacles OR predisposing factors OR enabling factors OR factors or precipitating factors OR reinforcing factors OR risk factors OR predictor or contributing factors or key factors or cause or correlation OR Factor, Risk OR Factors, Risk OR Risk Factor OR Population at Risk OR Risk, Population at OR Populations at Risk OR Risk, Populations at OR Causalities OR Multifactorial Causality OR Causalities, Multifactorial OR Causality, Multifactorial OR Multifactorial Causalities OR Multiple Causation OR Causation, Multiple OR Causations, Multiple OR Multiple Causations OR Reinforcing Factors OR Factor, Reinforcing OR Factors, Reinforcing OR Reinforcing Factor OR Causation OR Causations OR Enabling Factors OR Enabling Factor OR Factor, Enabling OR Factors, Enabling OR Predisposing Factors OR Factor, Predisposing OR Factors, Predisposing OR Predisposing Factor)
AND

Asthma control test OR Asthma control questionnaire OR ACT OR ACQ OR asthma control surveys OR asthma control assessment tool OR ACQ composite score OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
AND
(MH "Asthma") OR "asthma" OR (MH "Asthma, Occupational") OR (MH "Asthma, Exercise-Induced") OR (MH "Status Asthmaticus")
AND
(MM "Africa+") OR "africa" OR (MH "Africa South of the Sahara") OR (MH "Africa, Western") OR (MH "Democratic Nursing Organisation of South Africa") OR (MH "Africa, Southern") OR (MH "Africa, Eastern") OR (MH "Africa, Northern") OR (MH "South Africa") OR (MH "Africa, Central") OR (MH "South African Nursing Council") OR (MH "Namibia") OR (MH "Yohimbe") OR (MH "Medicine, African Traditional") OR (MH "Guinea") OR (MH "Ghana") OR (MH "Gabon") OR (MH "Ethiopia") OR (MH "Eritrea") OR (MH "Equatorial Guinea") OR (MH "Egypt") OR (MH "Djibouti") OR (MH "Democratic Republic of the Congo") OR (MH "Cote d'Ivoire") OR (MH "Botswana") OR (MH "Burkina Faso") OR (MH "Burundi") OR (MH "Cameroon") OR (MH "Cape Verde") OR (MH "Central African Republic") OR (MH "Algeria") OR (MH "Benin")

Table S2 NEWCASTLE OTTAWA QUALITY ASSESSMENT of included studies. Taken from: PA Modesti et al., (2016) .[16]

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (adapted for cross sectional studies)	Ayuk et al. 2018	Garba et al. 2014	Mpairwe et al. 2019
Selection: (Maximum 5 stars)			
1) Representativeness of the sample:			
a) Truly representative of the average in the target population. * (all subjects or random sampling)	★	★	★
b) Somewhat representative of the average in the target population. * (non-random sampling)			
c) Selected group of users.			
d) No description of the sampling strategy.			
2) Sample size:			★
a) Justified and satisfactory. *	★		★
b) Not justified.		0	
3) Non-respondents:			
a) Comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory. *			
b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.			
c) No description of the response rate or the characteristics of the responders and the non-responders.	0	0	
4) Ascertainment of the exposure (risk factor):			
a) Validated measurement tool. **	★ ★		★ ★
b) Non-validated measurement tool, but the tool is available or described. *		★	
c) No description of the measurement tool.			
Comparability: (Maximum 2 stars)			
1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.			
a) The study controls for the most important factor (select one). *	0	0	★
b) The study control for any additional factor. *	0	0	★
Outcome: (Maximum 3 stars)			
1) Assessment of the outcome:			
a) Independent blind assessment. **	★ ★	★ ★	★ ★
b) Record linkage. **			
c) Self-report. *			
d) No description.			
2) Statistical test:			
a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *	★	★	★
b) The statistical test is not appropriate, not described or incomplete.			
TOTAL	★7	★5	★10

16. Modesti PA, Reboldi G, Cappuccio FP, et al. Panethnic differences in blood pressure in Europe: a systematic review and meta-analysis. PloS one. 2016;11(1):e0147601. doi: 10.1371/journal.pone.0147601

Table S3 Barriers that impact asthma control in African children

Key:

Notes on this table:

- The study data has been grouped into thematic factors with multiple barriers; therefore, studies appear multiple times.
- Within each thematic factor, the studies are listed by the study design, quality score, size and the barriers they present.
- Barriers are colour coded according to the key below

Barriers associated with uncontrolled asthma	
Barriers that have null effect	
Complex or difficult to interpret	

Abbreviations

y	years	SPT	skin prick test	n	number of children
F	female	FeNo	fractional exhaled nitric oxide	x	number with outcome
M	male			N	number of children in population
				OR	odds ratio
				AMD	adjusted Mean difference
				m	missing
ICS	inhaled bronchodilator	AR	allergic rhinitis	CS	cross-sectional
SABA	short-acting beta-agonist	ETS	environmental tobacco smoke		
CA	controlled asthma	ACT	asthma control test	%	percent
UA	uncontrolled asthma				

Patient-related factors									
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Age									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] 5-12 y n=338 13-17 y n=214 Age 5-18 y	AMD	13 -17 y	-1.07	-1.20 to -0.94 P < 0.0001	5-12 y	Multivariate analysis	Sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy,	
Garba 2014 CS 6/10	South Africa N=115 15-18y n=23 10-14y n=54 Age 4-19 y	x/n (%)	15-18 y	15-18y 11(47.8%) UA vs 10-14y 25(46.3%) UA	NS	10-14 y	χ^2 test	None	
Gender									
Mpairwe H 2019 CS 10/10	Uganda N=561 [m=8] F n=292 M n=261 Age 5-18 y	OR	F	-0.54	NS	M	Multivariate analysis	Age, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy,	
Garba 2014 CS 6/10	South Africa N=115 F n=56 M n=59 Age 4-19 y	x/n (%)	F	F 26 (46.4%) UA vs M 25 (42.4%) UA	NS	M	χ2test	None	
Asthma medication use									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Inhaled SABA Yes 100 (18.1%)	51 (16.6%) CA vs 49 (19.9%) UA	NS		χ2test	No information	
			ICS Yes 37 (6.7%)	22 (7.2%) CA vs 15 (6.10%) UA	NS			No information	
			Steroid tablets Yes 149 (27.0%)	86 (28.1%) CA vs 63 (25.6%) UA	NS			No information	
			Neither salbutamol nor steroids Yes 225 (40.7%)	153 (49.8%) CA vs 72 (22.6%) UA	<0.0001		χ2test	No information	Mpairwe et al. noted that of 307 children with well-controlled asthma, 153 (49.8%) reported not using salbutamol or steroids in any formulation, they suggested that perhaps they had mild asthma.
Ethnicity									
Garba 2014 CS 6/10	South Africa N=115 CA n=64 UA n=51 Age 4-19	x/n (%)	Black n= 99 (86.1%) Coloured n= 7(6.1%) White n= 5 (4.3%) Asian n= 4 (3.5%)	Black race 53 (82.1%) CA vs Black race 46 (90.2%) UA	NS		χ2test	None	

Environmental related factors									
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
City residence									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] Rural n=71 Town n=433 City n=49 Ages 5-18y	OR	City dwelling in the first five years of life	-1.99	-3.69 to -0.29 p=0.02	Rural residence	Multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, concurrent allergy	Mpairwe et al. notes that p-value = 0.06 was for town and city and p-value= 0.02 for city only.
Ayuk A 2018 CS 6/10	Nigeria N=207 Urban n=178 Rural n=28 Ages 4-18y	x/n (%)	Urban residence	Urban 56 (31.4%) UA vs Rural 9 (32.1%) UA	NS	Rural residence	Fisher's exact test	No information	
Triggers (Home)									
Garba B 2014 CS 6/10	South Africa N=115 CA n=64 UA n=51 Age 4-19	x/n (%)	Dust n= 46 (40%)	25 (54.3%) CA vs 21 (45.7%) UA	NS		χ2test	None	
			Cockroach n= 39 (33.9%)	19 (48.7%) CA vs 20 (51.3%) UA	NS		χ2test	None	
			Carpet n= 38 (33.0%)	17 (44.7%) CA vs 21 (55.3%) UA	NS		χ2test	None	
			Pets n=26 (22.6%)	15 (57.7%) CA vs 11 (42.3%) UA	NS		χ2test	None	
			Toys in bed n= 20 (17.4%)	9 (45.0%) CA vs 110 (55.0%) UA	NS		χ2test	None	
			ETS n= 13 (11.3%)	6 (46.2%) CA vs 7 (53.8%) UA	NS		χ2test	None	

	Healthcare-related factors								
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Access to medication									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	ICS Yes n=37 (6.7%)	22 (7.2%) CA vs 15 (6.10%) UA	NS	Well-controlled asthma	χ2test	No information	
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Inhaled SABA Yes n=100 (18.1%)	51 (16.6%) CA vs 49 (19.9%) UA	NS	Well-controlled asthma	χ2test	No information	
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Neither salbutamol nor steroids Yes n=225 (40.7%)	153 (49.8%) CA vs 72 (29.3%) UA	p < 0.0001	Well controlled asthma	χ2test	No information	Mpairwe et al. noted that of 307 children with well-controlled asthma, 153 (49.8%) reported not using salbutamol or steroids in any formulation, they suggested that perhaps they had mild asthma.
Skin prick test									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] ACT test scores N=553 [m=9] Negative n=244 Positive n=300 Ages 5-18y	OR	Positive SPT ≥3mm	-0.51	-1.31 to 0.29 NS	Negative SPT <3mm	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy	
Fractional nitric oxide									
Mpairwe H 2019 CS 10/13	Uganda N= 561 ACT test scores N=553 [m=13] Normal n=335 Elevated n=195 Ages 5-18y	OR	Elevated value FeNo ≥ 35ppb	0.42	-0.39 to 1.24 NS	Normal value FeNo <35ppb	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy	

	Comorbidities								
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Allergy									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] ACT test scores N=553 [m=1] No n=434 Yes n=118 Ages 5-18y	OR	Concurrent AR	-1.33	-2.28 to -0.38 p= 0.006	No concurrent allergy	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city)	
Ayuk A 2018 CS 6/10	Nigeria N=207 No n=121 Yes n=86 Ages 4-18y	x/n (%)	Current allergy	Current allergy 26 (30.2%) UA vs No Allergy 38 (31.4%) UA	NS	No current allergy	Fisher's exact test	No information	

Systematic review

To edit the record click *Start an update* below. This will create a new version of the record - the existing version will remain unchanged.

1. * Review title.

Give the title of the review in English

Barriers associated with poor asthma control in children and adolescents in Africa: a systematic review

2. Original language title.

For reviews in languages other than English, give the title in the original language. This will be displayed with the English language title.

3. * Anticipated or actual start date.

Give the date the systematic review started or is expected to start.

18/05/2020

4. * Anticipated completion date.

Give the date by which the review is expected to be completed.

31/12/2020

5. * Stage of review at time of this submission.

Tick the boxes to show which review tasks have been started and which have been completed.
Update this field each time any amendments are made to a published record.

Reviews that have started data extraction (at the time of initial submission) are not eligible for inclusion in PROSPERO.
If there is later evidence that incorrect status and/or completion date has been supplied, the published PROSPERO record will be marked as retracted.

This field uses answers to initial screening questions. It cannot be edited until after registration.

The review has not yet started: No

Review stage	Started	Completed
Preliminary searches	Yes	Yes
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Provide any other relevant information about the stage of the review here.

6. * Named contact.

The named contact is the guarantor for the accuracy of the information in the register record. This may be any member of the review team.

Reratilwe Mphahlele

Email salutation (e.g. "Dr Smith" or "Joanne") for correspondence:
Dr Mphahlele

7. * Named contact email.

Give the electronic email address of the named contact.

mphahleler@ukzn.ac.za

8. Named contact address

PLEASE NOTE this information will be published in the PROSPERO record so please do not enter private information, i.e. personal home address

Give the full institutional/organisational postal address for the named contact.

719 Umbilo Road, Congella, 4013

9. Named contact phone number.

Give the telephone number for the named contact, including international dialling code.

0312604345

10. * Organisational affiliation of the review.

Full title of the organisational affiliations for this review and website address if available. This field may be completed as 'None' if the review is not affiliated to any organisation.

University of KwaZulu Natal

Organisation web address:
www.ukzn.ac.za

11. * Review team members and their organisational affiliations.

Give the personal details and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.
NOTE: email and country now MUST be entered for each person, unless you are amending a published record.

Dr Reratilwe Mphahlele. University of KwaZulu Natal
Professor Refiloe Masekela. University of KwaZulu Natal
Dr Omolemo Kitchin. University of Pretoria

12. * Funding sources/sponsors.

Details of the individuals, organizations, groups, companies or other legal entities who have funded or sponsored the review.

No funding has been secured for this review.

Grant number(s)
State the funder, grant or award number and the date of award
Not applicable

13. * Conflicts of interest.

List actual or perceived conflicts of interest (financial or academic).

None

14. Collaborators.

Give the name and affiliation of any individuals or organisations who are working on the review but who are not listed as review team members. **NOTE: email and country must be completed for each person, unless you are amending a published record.**

15. * Review question.

State the review question(s) clearly and precisely. It may be appropriate to break very broad questions down into a series of related more specific questions. Questions may be framed or refined using PI(E)COS or similar where relevant.

We interested in the determinants and barriers associated with poor asthma control in children and adolescents in Africa.

16. * Searches.

State the sources that will be searched (e.g. Medline). Give the search dates, and any restrictions (e.g. language or publication date). Do NOT enter the full search strategy (it may be provided as a link or attachment below.)

The evidence gathering will have 2 components:

16.1 Searching databases

The databases will include PubMed, Scopus, EBSCOhost (CINAHL, PsycINFO, MEDLINE) and Web of Science. Only scientific articles written in English with date restrictions from January 2000 to May 2020 will be included.

16.2 Hand Searching

Further hand searching will be conducted on Sabinet, African Journal online and Google Scholar.

17. URL to search strategy.

Upload a file with your search strategy, or an example of a search strategy for a specific database, (including the keywords) in pdf or word format. In doing so you are consenting to the file being made publicly accessible.

Or provide a URL or link to the strategy. Do NOT provide links to your search **results**.

https://www.crd.york.ac.uk/PROSPEROFILES/196755_STRATEGY_20200702.pdf

Do not make this file publicly available until the review is complete

18. * Condition or domain being studied.

Give a short description of the disease, condition or healthcare domain being studied in your systematic review.

The global prevalence of asthma is on the rise from an estimated 235 million in 2011 to around 340 million people affected today. Although we are beginning to see a plateau of the asthma epidemic in developed countries, there is a continuing increase in Low- and middle-income countries (LMICs) where adults and children suffer disproportionately from severe asthma. In Africa, the number of adolescents suffering from severe asthma symptoms is higher than the global average. To date, the lack of asthma research and infrastructure in LMICs means few studies focus on identifying the reasons for uncontrolled asthma in children. However, a recent report from Global Asthma Network (GAN) suggested that asthma control is poor in African children due to lack of diagnosis, insufficient asthma management infrastructure, lack of asthma knowledge and stigma.

Barriers to optimal asthma control are primarily grouped into patient-related factors (e.g. treatment adherence, perception and attitude towards asthma), environmental factors (e.g. pollution, tobacco smoke and biomass fuels), healthcare-related (e.g. availability of treatment and healthcare facilities) and doctor-related factors (e.g. asthma knowledge and time spent on asthma education). Commonly used validated tools for asthma control assessment are the Asthma Control Test (ACT) and the Asthma Control Questionnaire (ACQ).

19. * Participants/population.

Specify the participants or populations being studied in the review. The preferred format includes details of both inclusion and exclusion criteria.

Children and adolescents between the ages 6-18 years with a doctors diagnosis of asthma or presumed diagnosis of asthma based on a history of recurrent wheeze; who have had a baseline prescription for asthma treatment. Studies with wider ranges of ages will be included if children aged 6-18 are reported separately or if >50% of the population are children within this age range

20. * Intervention(s), exposure(s).

Give full and clear descriptions or definitions of the interventions or the exposures to be reviewed. The preferred format includes details of both inclusion and exclusion criteria.

Observational studies that aim to identify exposure such as below:

Any environmental exposure:
Pollution (indoor and outdoor), environmental tobacco smoke, mould, biomass fuels, pets, physical exercise, sedentary lifestyle, antibiotic use, paracetamol use, industrial combustion, respiratory infections.

Patient-related factors:
Attitudes, knowledge and perceptions, adherence, beliefs, inhaler technique, lifestyle, relationships, communication

Healthcare and Doctor related:
Availability of treatment and healthcare facilities, doctor asthma knowledge, time spent on asthma education, availability of medications,

21. * Comparator(s)/control.

Where relevant, give details of the alternatives against which the intervention/exposure will be compared (e.g. another intervention or a non-exposed control group). The preferred format includes details of both inclusion and exclusion criteria.

Where applicable:
Usual care in people of the same age with well-controlled asthma

22. * Types of study to be included.

Give details of the study designs (e.g. RCT) that are eligible for inclusion in the review. The preferred format includes both inclusion and exclusion criteria. If there are no restrictions on the types of study, this should be stated.

Cohort, case-control, cross-sectional studies. Studies looking at factors associated with asthma control as measured by child ACT/ACT and/or ACQ.

23. Context.

Give summary details of the setting or other relevant characteristics, which help define the inclusion or exclusion criteria.

Research with a focus on identifying barriers associated with poor asthma control in African children aged 6-18 with diagnosed/suspected asthma where asthma control is measured by ACT/ACQ will be included. The studies should be in English and published from January 2000 to May 2020 to ensure the encompassing of all data since the validation of the ACT and ACQ. Clinical trials or randomized control studies assessing interventions, pharmaceutical treatment as well as diagnostic accuracy of tools will also be excluded. Grey literature from experts in the field, conference abstracts or unpublished material will be excluded.

24. * Main outcome(s).

Give the pre-specified main (most important) outcomes of the review, including details of how the outcome is defined and measured and when these measurement are made, if these are part of the review inclusion criteria.

Our main outcome is poorly controlled asthma as measured by a Child ACT / ACT score of ≤19 and/or ACQ score of ≥1.

Measures of effect
We would like to identify factors associated with poor asthma control measured either in relative or absolute terms.

25. * Additional outcome(s).

List the pre-specified additional outcomes of the review, with a similar level of detail to that required for main outcomes. Where there are no additional outcomes please state 'None' or 'Not applicable' as appropriate to the review

None

Measures of effect

Not applicable

26. * Data extraction (selection and coding).

Describe how studies will be selected for inclusion. State what data will be extracted or obtained. State how this will be done and recorded.

Records that have been identified by the searches will be uploaded to Endnote for duplicate screening and removal. Reasons for exclusion and inclusion will be recorded using bibliographic details. Two reviewers will independently review the full texts of included records, where discrepancies are found a third reviewer will arbitrate to reach an agreement. After gathering the data, all references will be independently screened by two reviewers using a 3-stage review of title and abstract, followed by a full-text review of included studies. The full texts of all studies found to be relevant, and meeting the inclusion criteria will be retained for the final synthesis. Data will be extracted using a standardized data extraction form that will include: publication suitability, authorship, design, analysis, findings and report. The process of the selection will be summarized using a PRISMA flow diagram.

27. * Risk of bias (quality) assessment.

State which characteristics of the studies will be assessed and/or any formal risk of bias/quality assessment tools that will be used.

Two reviewers will independently perform a quality appraisal of all included studies, in case of disagreements, a third reviewer will assist in resolving differences. Quality of the non-randomized studies will be assessed using the Newcastle-Ottawa Scale for cohort, case studies and cross-sectional studies which takes into account selection, comparability and outcome fields.

28. * Strategy for data synthesis.

Describe the methods you plan to use to synthesise data. This **must not be generic text** but should be **specific to your review** and describe how the proposed approach will be applied to your data.
If meta-analysis is planned, describe the models to be used, methods to explore statistical heterogeneity, and software package to be used.

We will provide a narrative synthesis along with a thematic framework of barriers associated with poor asthma control with detailed tables. The framework for synthesis will consist of the following elements:

1. Familiarization with data against the aims of the review to:

a. Develop a list of exposures and environmental influences that quantitatively contribute to poor asthma control.

b. Identify a thematic framework based on emerging themes from observational studies to offer a list of likely factors that contribute to poor asthma control.

2. Exploring relationships and association within and between studies.

We expect heterogeneity among the studies, and this will limit the ability to perform a meta-analysis.

29. * Analysis of subgroups or subsets.

State any planned investigation of 'subgroups'. Be clear and specific about which type of study or participant will be included in each group or covariate investigated. State the planned analytic approach.

None planned

30. * Type and method of review.

Select the type of review, review method and health area from the lists below.

Type of review

Cost effectiveness	No
Diagnostic	No
Epidemiologic	No
Individual patient data (IPD) meta-analysis	No
Intervention	No
Living systematic review	No

Meta-analysis	No
Methodology	No
Narrative synthesis	No
Network meta-analysis	No
Pre-clinical	No
Prevention	No
Prognostic	No
Prospective meta-analysis (PMA)	No
Review of reviews	No
Service delivery	No
Synthesis of qualitative studies	No
Systematic review	Yes
Other	No

Health area of the review

Alcohol/substance misuse/abuse	No
Blood and immune system	No
Cancer	No
Cardiovascular	No
Care of the elderly	No
Child health	Yes
Complementary therapies	No
COVID-19	No
Crime and justice	No
Dental	No
Digestive system	No
Ear, nose and throat	No
Education	No
Endocrine and metabolic disorders	No
Eye disorders	No

General interest	No
Genetics	No
Health inequalities/health equity	No
Infections and infestations	No
International development	No
Mental health and behavioural conditions	No
Musculoskeletal	No
Neurological	No
Nursing	No
Obstetrics and gynaecology	No
Oral health	No
Palliative care	No
Perioperative care	No
Physiotherapy	No
Pregnancy and childbirth	No
Public health (including social determinants of health)	No
Rehabilitation	No
Respiratory disorders	Yes
Service delivery	No
Skin disorders	No
Social care	No
Surgery	No
Tropical Medicine	No
Urological	No
Wounds, injuries and accidents	No
Violence and abuse	No

31. Language.

Select each language individually to add it to the list below, use the bin icon to remove any added in error.

English

There is not an English language summary

32. * Country.

Select the country in which the review is being carried out. For multi-national collaborations select all the countries involved.

South Africa

33. Other registration details.

Name any other organisation where the systematic review title or protocol is registered (e.g. Campbell, or The Joanna Briggs Institute) together with any unique identification number assigned by them.
If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.

34. Reference and/or URL for published protocol.

If the protocol for this review is published provide details (authors, title and journal details, preferably in Vancouver format)

No I do not make this file publicly available until the review is complete

35. Dissemination plans.

Do you intend to publish the review on completion?

Yes

The completed review will be submitted to a peer-review journal for publication. A report will be collated for stakeholders who intend on developing focused interventions in an African setting.

36. Keywords.

Give words or phrases that best describe the review. Separate keywords with a semicolon or new line. Keywords help PROSPERO users find your review (keywords do not appear in the public record but are included in searches). Be as specific and precise as possible. Avoid acronyms and abbreviations unless these are in wide use.

asthma control
Asthma Control Test
ACT
Child asthma control test
(C)ACT
Asthma Control Questionnaire
ACQ
Africa
Child
Adolescent
Predictors
Risk Factors
uncontrolled asthma
Asthma

37. Details of any existing review of the same topic by the same authors.

If you are registering an update of an existing review give details of the earlier versions and include a full bibliographic reference, if available.

38. * Current review status.

Update review status when the review is completed and when it is published.
New registrations must be ongoing so this field is not editable for initial submission.

Review_Ongoing

39. Any additional information.

Provide any other information relevant to the registration of this review.

40. Details of final report/publication(s) or preprints if available.

Leave empty until publication details are available OR you have a link to a preprint (NOTE: this field is not editable for initial submission).
List authors, title and journal details preferably in Vancouver format.

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Pg 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pg 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pg 3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pg4-5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pg 4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pg 4 Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pg5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pg 4,5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pg 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 5,6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Table S3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pg 4,5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pg 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table S3
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pg 5,7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pg 5,7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Table S2
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pg 6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Pg 6
Study characteristics	17	Cite each included study and present its characteristics.	Pg 6,7
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pg 7, Table 2, Table S2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table S3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pg 5,7
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table S3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pg 10-13
	23b	Discuss any limitations of the evidence included in the review.	Pg 12
	23c	Discuss any limitations of the review processes used.	Pg 12
	23d	Discuss implications of the results for practice, policy, and future research.	Pg 12,13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Pg 2
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pg 2
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pg 13
Competing interests	26	Declare any competing interests of review authors.	Pg 14
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Pg 14

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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Title: Barriers and determinants of asthma control in children and adolescents in Africa: A systematic review.

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ABSTRACT

Objective: To identify reasons for poor asthma control in African children and adolescents.

Design: Systematic review

Data sources: PubMed, Scopus, CINHAL, PsycINFO, MEDLINE and Web of Science databases were systematically searched up to 31 May 2020. Hand searching was done on Sabinet, African Journal online and Google Scholar.

Eligibility Criteria: Studies identifying barriers to asthma control, where asthma control was assessed by the validated Asthma control test (c-ACT/ACT) and/or Asthma control questionnaire (ACQ) were included.

Data extraction and synthesis: Two reviewers independently selected studies for inclusion with disagreements resolved by a research team discussion, including a third reviewer. Data was extracted using the Cochrane Effective Practice and Organization of Care data collection form**.** The quality of the included studies was assessed using the modified Newcastle-Ottawa quality assessment scale. Identified barriers were reported in a thematic narrative synthesis.

Primary outcomes: Poorly controlled asthma and associated factors.

Results: From 914 records, three studies conducted between 2014 and 2019 in Nigeria, Uganda and South Africa met the inclusion criteria. A total of 883 children aged 4 - 19 years were analysed. Older age, concurrent allergy and city-dwelling significantly impacted asthma control. Few children with asthma symptoms in the

community had ever used inhaled corticosteroids (6,7%) and identified reasons included lack of asthma diagnosis (38,8%) and no prescribed treatment (47,6%).

Conclusion: Asthma control in African children is impacted by age, allergy, urbanisation and lack of access to asthma diagnosis and treatment. More studies focusing on identifying barriers to asthma control in Africa are needed.

PROSPERO (registration no. CRD42020196755)

KEYWORDS: urbanisation, access to care, community-based research, asthma outcomes, public health, air quality, low-and-middle-income countries

Strength and limitations

- This systematic review highlights the paucity of studies on barriers and determinants of asthma control in Africa.
- The sufficiently validated ACT/cACT was used to assess asthma outcomes and identify barriers to asthma control.
- Barriers to asthma control reported in this study contribute to, and match those described in the literature on paediatric asthma.
- A limitation of this study is that the heterogeneity of the studies precluded a meta-analysis.

INTRODUCTION

Asthma is a chronic non-communicable respiratory disease. According to the 2018 Global Asthma Report, asthma affects over 340 million people worldwide, the majority of whom reside in low-and-middle-income countries (LMICs). [1] In contrast to many high-income countries (HICs), the prevalence of asthma is steadily increasing in

LMICs, particularly in Africa.[1] The latest systematic review on asthma prevalence in Africa shows that compared to 74 million in 1990, by 2010, asthma affected 119 million of the total population. Of concern, nearly half of these asthma cases were children under 15 years.[2] Countries with the highest childhood asthma prevalence in Africa, South Africa (20.7%), Congo (19.9%), and Ivory Coast (19.3 %), are also regions with increasing urbanisation rates. [3 4] Factors associated with urbanisation including poverty, poor air quality and lifestyle and dietary changes may drive the rising asthma rate and impact asthma control.[5] However, in this setting, access to asthma healthcare and diagnosis as well as asthma research and research infrastructure remain lacking. [6-9]

The most commonly used validated tools for asthma control assessment are the composite score instruments; Asthma Control Test (ACT), Child Asthma Control Test (cACT) and the Asthma Control Questionnaire (ACQ). [10] The ACT and ACQ provide a quantitative assessment of asthma control and have been designated as core measures by the National Institutes of Health (NIH) for clinical research and observational studies.[10 11] ACT and ACQ are simple methods that can help quantify the impact of barriers on asthma control, [12] which may not be comparable between HICs and LMICs. [13] This review was conducted to collate data on reported barriers to asthma control in children and adolescents in Africa.

METHODS

The systematic review is registered with PROSPERO (registration no. CRD42020196755). We used the PECO acronym to aid with the systematic search. The preferred reporting items for systematic reviews and meta-analyses (PRISMA)

reporting standards were followed. [14] The Synthesis Without Meta-analysis reporting items guideline was used in conjunction with the PRISMA. [15]

Search strategy

The following databases were searched: PubMed, Scopus, CINHAL, PsycINFO, MEDLINE and Web of Science. The search methodology for all the databases is provided in the supplementary material (Table S1). Hand searching of the following databases was also conducted: Sabinet, African Journal online and Google Scholar. Only scientific articles written in English with date restrictions from 01 January 2000 to 31 May 2020 were included.

The search strategy was structured to include terms for "Child", "Asthma", "Barriers", "Asthma Control Test", "Africa" and or variations of these.

Selection of studies

Studies identified from searching electronic databases were combined, and duplicates were removed. Two reviewers (REM, OK) independently screened references using a 3-stage review of title and abstract, followed by a full-text review of included studies. The full text of potentially eligible studies was screened against the review criteria and potential articles identified. At each stage, disagreements were resolved by a team discussion with a third reviewer (RM).

Inclusion and exclusion criteria

The study's focus was to identify barriers associated with poor asthma control in African children and adolescents with doctor-diagnosed/suspected asthma, where the validated ACT/cACT or ACQ tool was used to assess asthma control. The population included children between the ages of 6 -18 years. Studies were included with broader

age ranges if children aged 6 -18 years were reported separately, or if >50% of the population were children within this age range.

Studies published from January 2000 to May 2020 were included to ensure the encompassing of all data since validation of the ACT and ACQ. Clinical trials assessing pharmaceutical treatment and diagnostic accuracy of tools were excluded. Grey literature from experts in the field, conference abstracts or unpublished material were also excluded. (Table 1.)

Table 1. Criteria for the search and rules devised to facilitate inclusion/exclusion criteria

Search strategy	Definition	Rules
Population	Children and adolescents between ages 6 -18 years with a doctor diagnosis or a baseline prescription for asthma treatment or presumed diagnosis of asthma based on a history of recurrent wheeze.	*Included* Studies with broader ranges of ages if children age 6-18 were reported separately or if >50% of the population were children within this age range. Excluded Studies in adults (>18years)
Exposure	Environmental related factors Pollution (indoor and outdoor), environmental tobacco smoke, mould, biomass fuels, pets, physical exercise, sedentary lifestyle, antibiotic use, paracetamol use, industrial combustion, respiratory infections. Patient-related factors Attitudes, knowledge and perceptions, adherence, beliefs, inhaler technique, lifestyle, relationships, communication Healthcare and doctor related factors	*Included* Studies aiming to identify exposures that had a quantifiable impact on asthma control. *Excluded:* • Clinical trials assessing pharmaceutical treatments. • Studies assessing the diagnostic accuracy of tools. • Studies assessing the validity of tools.

	Availability of treatment and healthcare facilities, doctor asthma knowledge, time spent on asthma education, availability of medications. Comorbidities Allergic Rhinitis, Obesity, Obstructive Sleep Apnoea (OSA) Gastroesophageal Reflux Disease (GERD)	
Comparison (if applicable):	Usual care in people of the same age with well-controlled asthma	
Outcome	Asthma control measured using ACT /cACT and/or ACQ	*Excluded* Studies using tools for measuring asthma control other than ACT/cACT and/or ACQ
Timeframe	20 years between January 2000 – May 2020	*Excluded* Studies conducted before January 2000 and after May 2020
Setting	Africa	*Excluded* Studies not done in Africa
Study	Cohort, case-control, cross-sectional	*Included* Studies identifying exposures that impact asthma control as measured by cACT/ ACT and/or ACQ

ACT: asthma control test; cACT: child asthma control test; ACQ: asthma control questionnaire

Data extraction

The full texts of all studies found to be relevant and meeting the inclusion criteria were retained for data extraction and final synthesis. Data including study design, setting, population, authorship and statistical analysis was extracted using a standardised data extraction form modified from the Cochrane Effective Practice and Organization of Care data collection form.[16] The authors were contacted where clarification was

required, and data was missing. The selection process was summarised using a PRISMA flow diagram (Figure 1).

Quality assessment

The included studies' quality was assessed using the modified Newcastle-Ottawa Scale for cohort, case studies, and cross-sectional studies. [17] (Table S2).

Data analysis and synthesis

We anticipated that the population and statistical analysis heterogeneity of the studies would preclude a formal meta-analysis. We, therefore, grouped into themes asthma control barriers corresponding to literature; patient, environmental, healthcare/doctor-related factors and comorbidities[12 13]. (Table S3). Statistical analyses were performed using MedCalc-Software, Ostend, Belgium; http://www.medcalc.org; 2018.[18]

Patient and public involvement

Patients and the public were not involved in the study design or conduction of the study.

RESULTS

Search Results

There were 914 articles identified: 863 articles through electronic database searching (EBSCO host = 27, PubMed = 136, Web of Science = 97, Scopus = 603) and an additional 51 articles through hand searching (Google scholar = 23, Sabinet = 12, AJOL = 16). The total number of articles found after duplicates were removed was 498. Of the 498 articles screened, 484 were excluded as they were not appropriate or

did not relate to the study. The remaining 14 full articles were assessed for eligibility, and 11 articles were excluded for the following reasons: wrong age group =2, Did not use ACT/ACQ = 2, not original research = 2, assessed impact rather than barriers of poor asthma control = 5. Three studies met the inclusion criteria. (Figure 1.)

[INSERT FIGURE 1 HERE]

Characteristics of the studies

All three studies conducted in Nigeria, South Africa and Uganda [19-21] were cross-sectional; two hospital-based and one community-based. The sample size was smaller for hospital-based studies with 207 and 115 participants in Nigeria[19] and South Africa[20], respectively, compared to the community-based study of 561 participants in Uganda.[21] Publication dates ranged from 2014 to 2019. The ages of participants ranged from 4 - 19 years. Asthma diagnosis was based on doctor diagnosis [19 20] guided by the Global Initiative on Asthma (GINA),[19] and symptom screening by the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. [21] One study adjusted for age, gender and concurrent allergy [21], while the rest did not report adjusting for potential confounders, reducing their quality score. [19 20] (Table S2) To recruit participants, two of the hospital-based studies used consecutive enrollment from a group of children attending asthma clinic.[19 20] The community-based study derived participants from a large case-control study investigating risk factors of asthma in school going children.[21 22] (Table 2)

Table 2. Characteristics of included studies

Author ref	Study type	Setting	Year of Publication	Country of origin	Sample Size	Age ranges (years)	Asthma definition	Asthma control definition	Recruitment	Exposures	Quality Score	Reviewers comment
Ayuk et al [19]	Cross sectional	Hospital	2018	Nigeria	207	4-18	Doctor Diagnosis, GINA	ACT / cACT >19 controlled <19 uncontrolled	Consecutive enrolment for 1 year from a group of children attending the asthma clinic	Family size, socioeconomic status, urban vs rural dwelling, allergy status (by ISAAC), Triggers (particulate and non-particulate)	7/10	Author contacted for further information on participant numbers.
Garba et al [20]	Cross sectional	Hospital	2014	South Africa	115	5-18	Doctor diagnosis	ACT / cACT = 25 (ACT)/ 27 (cACT) total control >19 well-controlled ≤ 19 uncontrolled 16-19 somewhat controlled <16 Poorly controlled	Consecutive enrolment for 4 months from a group of children attending the asthma clinic	Presence of a smoker at home, presence of pets, cockroaches and use of biomass fuel, the child's sleeping environment (dust, carpets and soft toys in the bedroom). Compliance with medications and inhaler technique. Allergy status (by clinical examination)	5/10	Author contacted for further information on recruitment strategy, data analysis and participant numbers.
Mpairwe et al [21]	Cross-sectional	Community School	2019	Uganda	561	5-17	Screening ISAAC questionnaire	ACT / cACT > 19 Well controlled 15-19 partly controlled <15 Poorly controlled	Recruitment from children with self-reported breathing problems at schools in an urban area	Age, sex, regular physical exercise as recommended by WHO, area of residence in 1st 5 years of life (rural, town or city), concurrent allergy, antimalarials	10/10	Describes participants as derived from a large case-control [22] study to investigate risk factors of asthma

WHO: world health organisation; ACT: asthma control test; cACT: child asthma control test; ISAAC: international survey on asthma and atopy in children; GINA: global initiative for asthma

22. Mpairwe H et al. Risk factors for asthma among schoolchildren who participated in a case-control study in urban Uganda. Elife. 2019;8:e49496.

Assessment of asthma control

All the studies measured asthma control using ACT and cACT. Scores were based on the cutoff point of >19 for controlled asthma and ≤ 19 for uncontrolled asthma. The prevalence of uncontrolled asthma in the Nigeria, South Africa and Uganda was 30.9%, 44.3% and 44.5% respectively.

Thematic synthesis

Patient-related factors

Age

Two studies assessed the impact of age on asthma control. The large community-based study showed that older age (13 -17 years) was significantly associated with poorer asthma control (-1.07 [-1.20, -0.94], p < 0.0001). [21] The exception was a small clinic cohort of moderate quality, which showed no association. [20]

Gender

Two of the studies [20 21] that examined gender showed no significant association with asthma control.

Asthma medication use

Two studies [20 21] examined the use and compliance of asthma medication. The study amongst school-going children [21] showed that the majority (73%) had never used inhaled asthma medications. Additionally, regular use of inhaled asthma medication in the last 12 months was inadequate for salbutamol (18.1%) and corticosteroid (6.7%) even though the majority (55.8%) had a doctor diagnosis of asthma. Although not significant, in the same cohort, children with poorly controlled asthma preferred regular use of (salbutamol and prednisone) tablets rather than inhaled salbutamol and

corticosteroids. [21] Conversely, in the cohort of children attending asthma clinic [20], good adherence to medications was seen in 82.6% of patients. In these doctor-diagnosed children, asthma control was significantly associated with good adherence to medication, where 37.9% and 62.1% of patients had uncontrolled asthma and controlled asthma, respectively (x^2=0.217, p=0.002). [20]

Ethnicity

There was no significant association between asthma control and ethnicity (x^2=3.22, p =0.359) in Black-African, Caucasian, Mixed-ethnicity and Indian participants in South Africa[20].

Environmental related factors

Two studies conducted in Uganda[21] and Nigeria[19] examined the effects of rural vs urban domicile on asthma control. The school-based Ugandan cohort showed that city residence in early life was associated with poor asthma control (-1.99[-3.69, -0.29], p =0.02). [21] In contrast the clinic-based cohort in Nigeria showed, although without significance, that within the rural community, more children with current allergies had better control of their asthma (85.7%) when compared to their urban counterparts (66.7%). Interestingly, the children who lived in rural areas *without* concurrent allergy had poorly controlled asthma (50.0%) compared to their urban counterparts (28.3%), Fisher's exact test =2.076, p= 0.17, although this too was not significant. [19]

All three included studies considered the presence of asthma triggers in their participants' environments, but only the South African study examined these triggers in relation to asthma control. Common triggers included dust, cold air, physical exercise, fumes or air pollution, pollen, pets, smoking and biomass fuels. (Figure 2.) In the South African cohort, home circumstances including dust, cockroach, carpet,

pets, toys in bed, and smoking were not found to be associated with asthma control. [20] The use of biomass fuel was uncommon in South Africa (6.1%) compared to Nigeria (22.1%) and was not found to be significantly associated with asthma control (x^2 =6.202, p =0.185). [19 20]

[INSERT FIGURE 2 HERE]

Healthcare and doctor related factors

Only the field-based study in Uganda, reported the impact of healthcare-seeking behaviour on asthma control. In 553 children who reported treating their asthma in the last year, 26.8% reported having ever used inhaled asthma medications, and a similar proportion, 29.7% reported having ever used herbal remedies for asthma management. On enquiry about previous asthma assessments and follow-up, 73 (13.2 %) visited a health facility to monitor their asthma, 45 (8.2%) children had ever had a lung function test; two (0.4%) had ever used a peak flow meter as an asthma monitoring tool at home, and only three (0.5%) had a personal written asthma action plan.[21] The reason for having never used inhaled asthma medication was investigated in 405 children and included: inhaled asthma medications had never been prescribed for them (47.6%), never been diagnosed (38.8%), high cost of inhalers (4.5%), fear of side effects of inhalers (4.5%), alternative treatment with salbutamol or steroid tablets (1.4%) and non-medicinal treatment, i.e. wrapping up in warm clothes and resting. [21]

Comorbidities

All three studies assessed children for allergic rhinitis, but only two [19 21] in relation to asthma control. In the larger powered community-based study, [21] children with concurrent allergic rhinitis were more likely to have lower asthma control scores (-1.33

[-2.28, -0.38], p=0.006), whereas no significant association was found between atopy and asthma control in the small cohort clinic-based study. [19] However, in the latter study, children with current allergy had more emergency hospital visits due to asthma exacerbations (x2 = 10.09 [df 1] p = 0.002; Spearman's R =0.22, p = 0.001). [19]

DISCUSSION

Older age, concurrent allergic rhinitis and early life urban residence are barriers similar to HICs and significantly impact asthma control in African children. Access to healthcare and appropriate asthma medication remains limited, with a minority of children with asthma symptoms ever having used ICS.

Older age

Mpairwe et al. found adolescents in Uganda have inadequate asthma control and outcomes. Similarly, the age group 12 -17 years was more predictive of exacerbations than other age groups in a European cohort study using the General Practice Research Database (GPRD) [23]. One reason for this can be explained by adolescent studies that show poor adherence compared to other age groups. [24] Social stigma, forgetfulness and poor understanding of medication play a significant role in adherence and warrant further exploration. [25 26]

Concurrent allergic rhinitis

The Ugandan and Nigerian studies found that children with AR had less well-controlled asthma and were more likely to be hospitalised. Similarly, in a large UK retrospective cohort of 9522 children with asthma, the presence of AR significantly increased the

likelihood of physician visits and more than doubled the likelihood of hospitalisation. Furthermore, drug use and costs were significantly higher among children with asthma and concurrent AR. [27] Active search and recognition of AR when assessing children remains critical in comprehensive asthma management.

Rural versus urban residence

Studies in Africa show a decreasing gradient in asthma prevalence between urban and rural areas [28 29]. In this context, biomass fuel exposure remains a significant contributor to inflammatory lung diseases, including asthma and chronic obstructive pulmonary disease (COPD). [30 31] Few studies in Africa have compared asthma control between rural and urban areas. [19 21 32 33] Urban residence was significantly associated with poorly controlled asthma in Uganda, where asthma risk among schoolchildren [21] was three times higher in children who in early life resided in cities rather than rural areas. [22] Similarly, rural to urban migration appears to be an important determinant of the increasing prevalence of wheeze among school-going children in Latin American cities. [34 35] Increasing asthma rates in peri-urban settings could be related to over-crowding, reduction of exercise, poorer air quality and changes in lifestyle and diets.

Access to diagnosis and health care

Six out of 10 children attending healthcare institutions have good asthma control, while a similar number of undiagnosed children in the community have poorly controlled asthma. [19-21] Even after a diagnosis of asthma, ICS use is limited in communities [21 36] compared to clinic patients [20] who once diagnosed, have significantly better asthma control. The preference of tablets (salbutamol and corticosteroids) over ICS may largely be explained by their quick relief and ease of administration combined with underlying suboptimal knowledge and asthma medications cost. [36] Furthermore,

traditional healers remain integral to medical care in communities due to local cultural practices and beliefs. There is a need to communicate asthma management strategies to communities in a culturally sensitive manner. [32] [37] Triggers including dust, air pollution, pollen, pets, and smoking common across the globe, indicate the feasibility of a global checklist and the necessity of avoidance education. [38]

Strengths and limitations

We may not have identified all significant barriers that impact asthma control as other asthma control tools, i.e. Global Initiative for Asthma (GINA) and National Asthma Education Programme (NAEP), were excluded because they are not as sufficiently validated as the ACT and ACQ.[10] Nevertheless, we identified variables in each group classification for poor asthma control in current literature.[13] Our wide-ranging search strategy found no non-English articles requiring exclusion. The studies' heterogeneity in terms of outcome analysis and population precluded a meta-analysis; therefore, we reported all the factors within the emerging themes.

Implications for clinical practice, healthcare systems and policymakers

Strategies that improve medication access, including initiatives like the WHO Essential Medicines List, low-cost equipment like plastic spacers [39] and implementing culturally appropriate educational programs for healthcare workers and the public, remain vital. [40] [41]

Implications for future research

Studies beyond healthcare institutions that include communities in identifying barriers and their impact on asthma control are needed in African children.

CONCLUSION

Asthma control barriers requiring focus in Africa are; lack of accurate diagnosis, limited access to inhaled therapy, lack of asthma knowledge and poor air quality. Better education and advocacy through community-based public interventions are needed to improve African children's asthma control and outcomes.

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Figure 1. Study eligibility chart according to PRISMA criteria.

Figure 2. Prevalence of asthma triggers among study participants across African studies using the ACT/cACT to identify asthma control barriers. ETS = environmental tobacco smoke. ACT = asthma control test. cACT= childhood asthma control test.

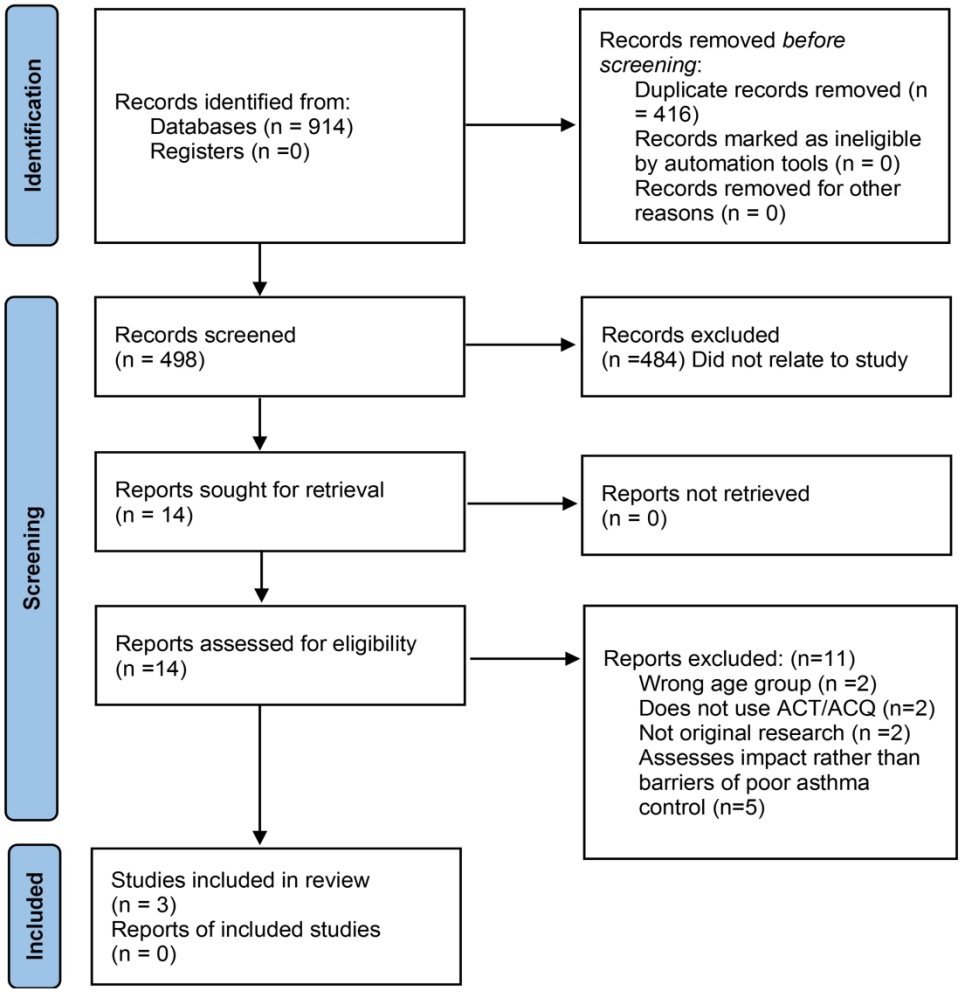

Figure 1. Study eligibility chart according to PRISMA criteria

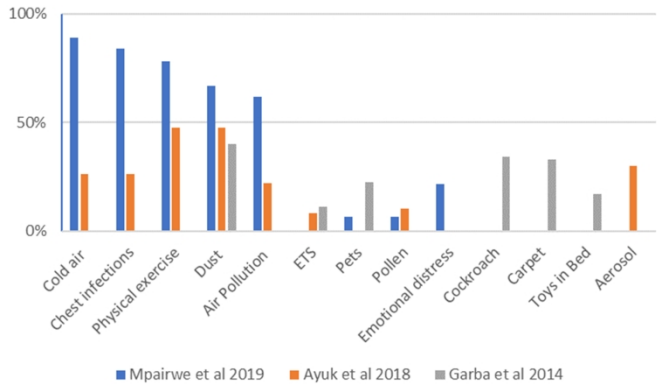

Figure 2. Prevalence of asthma triggers among study participants across African studies using the ACT/cACT to identify asthma control barriers. ETS = environmental tobacco smoke. ACT = asthma control test. cACT= childhood asthma control test.

338x190mm (300 x 300 DPI)

Table S1 SEARCH STRINGS Asthma control barriers in African children.

PUBMED SEARCH STRING

pediatric* or paediatric* or child* or kindergarten* or kindergarden* or "elementary school*" or schoolchild* or boy or boys or girl* or "middle school*" or pubescen* or juvenile* or teen* or youth* or "high school*" or adolesc* or pre-pubesc* or prepubesc*) OR (child* or adolesc* or pediat* or paediat* [Journal]) OR child[MeSH Terms] OR infant[MeSH Terms] OR adolescent[MeSH Terms] OR pediatrics[MeSH Terms] OR minors[MeSH Terms]
AND
Asthma control test OR Asthma control questionnaire OR ACT OR ACQ OR asthma control surveys OR asthma control assessment tool OR ACQ composite score OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
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SCOPUS SEARCH STRING

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AND
"Asthma*" OR "Bronchial Asthma" OR "Bronchial" AND "Asthma" OR "Bronchial Asthma, Exercise Induced" OR "Exercise Induced Bronchial Asthma*" OR "Asthma*, Exercise-Induced" OR "Exercise Induced Asthma" OR "Exercise-Induced Asthma*" OR "Bronchospasm, Exercise-Induced" OR "Bronchospasm*, Exercise Induced" OR "Exercise-Induced Bronchospasm*" OR "Exercise Induced Bronchospasm" OR "Bronchial Spasm*" OR "Spasm*, Bronchial" OR "Bronchospasm*" OR "Wheez*" OR "Status Asthmaticus" OR "Bronchial Hyperreactivit*" OR "Respiratory Hypersensitivit*" OR "Bronchoconstrict*"
AND
"Asthma control test" OR "Asthma control questionnaire" OR ACT OR "Childhood asthma control test" OR C-ACT OR ACQ OR "asthma control survey*" OR "asthma control assessment tool" OR "ACQ composite score" OR ACQ5 OR ACQ6 OR ACQ-FEV1 OR ACQ-PEF OR ACQ-wLF
AND
Challenge* OR Problem* OR Barriers OR Difficult* OR Issue* or Limitation* OR Obstacle* OR "predisposing factor*" OR "enabling factor*" OR factors OR "precipitating factor*" OR "reinforcing factor*" OR "risk factor*" OR predictor OR "contributing factor*" OR "key factor*" OR caus* OR correlation* OR "Factor, Risk" OR "Factors, Risk" OR "Risk Factor" OR "Population at Risk" OR "Risk, Population" at OR "Populations at Risk" OR "Risk, Populations at" OR Causalities OR "Multifactorial Causality" OR "Causalities, Multifactorial" OR "Causality, Multifactorial" OR "Multifactorial Causalities" OR "Multiple Causation" OR "Causation, Multiple" OR "Causations, Multiple" OR "Multiple Causations" OR "Reinforcing Factors" OR "Factor, Reinforcing" OR" Factors, Reinforcing" OR "Reinforcing Factor" OR Causation* OR "Enabling Factor*" OR "Enabling Factor" OR "Factor, Enabling" OR "Factor*, Enabling" OR "Predisposing Factor*" OR "Factor, Predisposing" OR" Factor*, Predisposing"
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((pediatric* or paediatric* or child* or kindergarten* or kindergarden* or "elementary school*" or schoolchild* or boy or boys or girl* or "middle school*" or pubescen* or juvenile* or teen* or youth* or "high school*" or adolesc* or pre-pubesc* or prepubesc*) OR (child* or adolesc* or pediat* or paediat* [Journal]) OR child[MeSH Terms] OR infant[MeSH Terms] OR adolescent[MeSH Terms] OR pediatrics[MeSH Terms] OR minors[MeSH Terms])) Search modes - Boolean/Phrase
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(MH "Asthma") OR "asthma" OR (MH "Asthma, Occupational") OR (MH "Asthma, Exercise-Induced") OR (MH "Status Asthmaticus")
AND
(MM "Africa+") OR "africa" OR (MH "Africa South of the Sahara") OR (MH "Africa, Western") OR (MH "Democratic Nursing Organisation of South Africa") OR (MH "Africa, Southern") OR (MH "Africa, Eastern") OR (MH "Africa, Northern") OR (MH "South Africa") OR (MH "Africa, Central") OR (MH "South African Nursing Council") OR (MH "Namibia") OR (MH "Yohimbe") OR (MH "Medicine, African Traditional") OR (MH "Guinea") OR (MH "Ghana") OR (MH "Gabon") OR (MH "Ethiopia") OR (MH "Eritrea") OR (MH "Equatorial Guinea") OR (MH "Egypt") OR (MH "Djibouti") OR (MH "Democratic Republic of the Congo") OR (MH "Cote d'Ivoire") OR (MH "Botswana") OR (MH "Burkina Faso") OR (MH "Burundi") OR (MH "Cameroon") OR (MH "Cape Verde") OR (MH "Central African Republic") OR (MH "Algeria") OR (MH "Benin")

Table S2 NEWCASTLE OTTAWA QUALITY ASSESSMENT of included studies. Taken from: PA Modesti et al., (2016) .[176]

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE (adapted for cross sectional studies)	Ayuk et al. 2018	Garba et al. 2014	Mpairwe et al. 2019
Selection: (Maximum 5 stars)			
1) Representativeness of the sample:			
a) Truly representative of the average in the target population. * (all subjects or random sampling)	★	★	★
b) Somewhat representative of the average in the target population. * (non-random sampling)			
c) Selected group of users.			
d) No description of the sampling strategy.			
2) Sample size:			★
a) Justified and satisfactory. *	★		★
b) Not justified.		0	
3) Non-respondents:			
a) Comparability between respondents and non-respondents' characteristics is established, and the response rate is satisfactory. *			
b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.			
c) No description of the response rate or the characteristics of the responders and the non-responders.	0	0	
4) Ascertainment of the exposure (risk factor):			
a) Validated measurement tool. **	★ ★		★ ★
b) Non-validated measurement tool, but the tool is available or described. *		★	
c) No description of the measurement tool.			
Comparability: (Maximum 2 stars)			
1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.			
a) The study controls for the most important factor (select one). *	0	0	★
b) The study control for any additional factor. *	0	0	★
Outcome: (Maximum 3 stars)			
1) Assessment of the outcome:			
a) Independent blind assessment. **	★ ★	★ ★	★ ★
b) Record linkage. **			
c) Self-report. *			
d) No description.			
2) Statistical test:			
a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *	★	★	★
b) The statistical test is not appropriate, not described or incomplete.			
TOTAL	★7	★5	★10

17. Modesti PA, Reboldi G, Cappuccio FP, et al. Panethnic differences in blood pressure in Europe: a systematic review and meta-analysis. PloS one. 2016;11(1):e0147601. doi: 10.1371/journal.pone.0147601

Table S3 Barriers that impact asthma control in African children

Key:

Notes on this table:

- The study data has been grouped into thematic factors with multiple barriers; therefore, studies appear multiple times.
- Within each thematic factor, the studies are listed by the study design, quality score, size and the barriers they present.
- Barriers are colour coded according to the key below

Barriers associated with uncontrolled asthma	
Barriers that have null effect	
Complex or difficult to interpret	

Abbreviations

y	years	SPT	skin prick test	n	number of children
F	female	FeNo	fractional exhaled nitric oxide	x	number with outcome
M	male			N	number of children in population
				OR	odds ratio
				AMD	adjusted Mean difference
				m	missing
ICS	inhaled bronchodilator	AR	allergic rhinitis	CS	cross-sectional
SABA	short-acting beta-agonist	ETS	environmental tobacco smoke		
CA	controlled asthma	ACT	asthma control test	%	percent
UA	uncontrolled asthma				

Patient-related factors									
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Age									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] 5-12 y n=338 13-17 y n=214 Age 5-18 y	AMD	13 -17 y	-1.07	-1.20 to -0.94 P < 0.0001	5-12 y	Multivariate analysis	Sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy,	
Garba 2014 CS 6/10	South Africa N=115 15-18y n=23 10-14y n=54 Age 4-19 y	x/n (%)	15-18 y	15-18y 11(47.8%) UA vs 10-14y 25(46.3%) UA	NS	10-14 y	χ^2 test	None	
Gender									
Mpairwe H 2019 CS 10/10	Uganda N=561 [m=8] F n=292 M n=261 Age 5-18 y	OR	F	-0.54	NS	M	Multivariate analysis	Age, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy,	
Garba 2014 CS 6/10	South Africa N=115 F n=56 M n=59 Age 4-19 y	x/n (%)	F	F 26 (46.4%) UA vs M 25 (42.4%) UA	NS	M	χ2test	None	
Asthma medication use									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Inhaled SABA Yes 100 (18.1%)	51 (16.6%) CA vs 49 (19.9%) UA	NS		χ2test	No information	
			ICS Yes 37 (6.7%)	22 (7.2%) CA vs 15 (6.10%) UA	NS			No information	
			Steroid tablets Yes 149 (27.0%)	86 (28.1%) CA vs 63 (25.6%) UA	NS			No information	
			Neither salbutamol nor steroids Yes 225 (40.7%)	153 (49.8%) CA vs 72 (22.6%) UA	<0.0001		χ2test	No information	Mpairwe et al. noted that of 307 children with well-controlled asthma, 153 (49.8%) reported not using salbutamol or steroids in any formulation, they suggested that perhaps they had mild asthma.
Ethnicity									
Garba 2014 CS 6/10	South Africa N=115 CA n=64 UA n=51 Age 4-19	x/n (%)	Black n= 99 (86.1%) Coloured n= 7(6.1%) White n= 5 (4.3%) Asian n= 4 (3.5%)	Black race 53 (82.1%) CA vs Black race 46 (90.2%) UA	NS		χ2test	None	

Environmental related factors									
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
City residence									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] Rural n=71 Town n=433 City n=49 Ages 5-18y	OR	City dwelling in the first five years of life	-1.99	-3.69 to -0.29 p=0.02	Rural residence	Multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, concurrent allergy	Mpairwe et al. notes that p-value = 0.06 was for town and city and p-value= 0.02 for city only.
Ayuk A 2018 CS 6/10	Nigeria N=207 Urban n=178 Rural n=28 Ages 4-18y	x/n (%)	Urban residence	Urban 56 (31.4%) UA vs Rural 9 (32.1%) UA	NS	Rural residence	Fisher's exact test	No information	
Triggers (Home)									
Garba B 2014 CS 6/10	South Africa N=115 CA n=64 UA n=51 Age 4-19	x/n (%)	Dust n= 46 (40%)	25 (54.3%) CA vs 21 (45.7%) UA	NS		χ2test	None	
			Cockroach n= 39 (33.9%)	19 (48.7%) CA vs 20 (51.3%) UA	NS		χ2test	None	
			Carpet n= 38 (33.0%)	17 (44.7%) CA vs 21 (55.3%) UA	NS		χ2test	None	
			Pets n=26 (22.6%)	15 (57.7%) CA vs 11 (42.3%) UA	NS		χ2test	None	
			Toys in bed n= 20 (17.4%)	9 (45.0%) CA vs 110 (55.0%) UA	NS		χ2test	None	
			ETS n= 13 (11.3%)	6 (46.2%) CA vs 7 (53.8%) UA	NS		χ2test	None	

	Healthcare-related factors								
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Access to medication									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	ICS Yes n=37 (6.7%)	22 (7.2%) CA vs 15 (6.10%) UA	NS	Well-controlled asthma	χ2test	No information	
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Inhaled SABA Yes n=100 (18.1%)	51 (16.6%) CA vs 49 (19.9%) UA	NS	Well-controlled asthma	χ2test	No information	
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] CA n=307 UA n=246 Age 5-18 y	x/n (%)	Neither salbutamol nor steroids Yes n=225 (40.7%)	153 (49.8%) CA vs 72 (29.3%) UA	p < 0.0001	Well controlled asthma	χ2test	No information	Mpairwe et al. noted that of 307 children with well-controlled asthma, 153 (49.8%) reported not using salbutamol or steroids in any formulation, they suggested that perhaps they had mild asthma.
Skin prick test									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] ACT test scores N=553 [m=9] Negative n=244 Positive n=300 Ages 5-18y	OR	Positive SPT ≥3mm	-0.51	-1.31 to 0.29 NS	Negative SPT <3mm	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy	
Fractional nitric oxide									
Mpairwe H 2019 CS 10/13	Uganda N= 561 ACT test scores N=553 [m=13] Normal n=335 Elevated n=195 Ages 5-18y	OR	Elevated value FeNo ≥ 35ppb	0.42	-0.39 to 1.24 NS	Normal value FeNo <35ppb	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city), concurrent allergy	

	Comorbidities								
Study ID, Design, Quality Score	**Country, Sample Size, Ages**	**Effect measure**	**Barrier definition**	**Effect value**	**95%CI or significance**	**Reference group or comparator**	**Analysis used**	**Adjustments or variables**	**Comments**
Allergy									
Mpairwe H 2019 CS 10/10	Uganda N= 561 [m=8] ACT test scores N=553 [m=1] No n=434 Yes n=118 Ages 5-18y	OR	Concurrent AR	-1.33	-2.28 to -0.38 p= 0.006	No concurrent allergy	multivariate analysis	Age, sex, regular physical exercise as recommended by WHO, area of residence 1st 5 years of life (rural, town or city)	
Ayuk A 2018 CS 6/10	Nigeria N=207 No n=121 Yes n=86 Ages 4-18y	x/n (%)	Current allergy	Current allergy 26 (30.2%) UA vs No Allergy 38 (31.4%) UA	NS	No current allergy	Fisher's exact test	No information	

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Pg 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Pg1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Pg 3-4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Pg 3-4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pg4-7
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Pg 4-7
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Pg 4-7 Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Pg7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Pg 4-7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pg 5-7,10
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Pg 5,6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Pg 8 Table S3
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Pg 4,5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Pg 5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table S3
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Pg 8
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Pg 8
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Table S2
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pg 8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Pg 8
Study characteristics	17	Cite each included study and present its characteristics.	Pg 10
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pg 8, Table 2, Table S2
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table S3
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Pg 10 Table 2
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Pg 10 Table S3
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table S3
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pg 14-17
	23b	Discuss any limitations of the evidence included in the review.	Pg 16-17
	23c	Discuss any limitations of the review processes used.	Pg 16-17
	23d	Discuss implications of the results for practice, policy, and future research.	Pg 16-17
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Pg 3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Pg 3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Pg 17
Competing interests	26	Declare any competing interests of review authors.	Pg 17
Availability of data, code and	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Pg 17

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
other materials			

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

For more information, visit: http://www.prisma-statement.org/

Synthesis Without Meta-analysis (SWiM) reporting items

The citation for the Synthesis Without Meta-analysis explanation and elaboration article is: Campbell M, McKenzie JE, Sowden A, Katikireddi SV, Brennan SE, Ellis S, Hartmann-Boyce J, Ryan R, Shepperd S, Thomas J, Welch V, Thomson H. Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guideline BMJ 2020;368:l6890 http://dx.doi.org/10.1136/bmj.l6890

SWiM is intended to complement and be used as an extension to PRISMA			
SWiM reporting item	**Item description**	**Page in manuscript where item is reported**	**Other***
Methods			
1 Grouping studies for synthesis	1a) Provide a description of, and rationale for, the groups used in the synthesis (e.g., groupings of populations, interventions, outcomes, study design)	pg 6	
	1b) Detail and provide rationale for any changes made subsequent to the protocol in the groups used in the synthesis		
2 Describe the standardised metric and transformation methods used	Describe the standardised metric for each outcome. Explain why the metric(s) was chosen, and describe any methods used to transform the intervention effects, as reported in the study, to the standardised metric, citing any methodological guidance consulted	pg 4 & 7	
3 Describe the synthesis methods	Describe and justify the methods used to synthesise the effects for each outcome when it was not possible to undertake a meta-analysis of effect estimates	pg 8	
4 Criteria used to prioritise results for summary and synthesis	Where applicable, provide the criteria used, with supporting justification, to select the particular studies, or a particular study, for the main synthesis or to draw conclusions from the synthesis (e.g., based on study design, risk of bias assessments, directness in relation to the review question)	pg 5-8	Table S2

Synthesis Without Meta-analysis (SWiM) reporting items

SWiM reporting item	Item description	Page in manuscript where item is reported	Other*
5 Investigation of heterogeneity in reported effects	State the method(s) used to examine heterogeneity in reported effects when it was not possible to undertake a meta-analysis of effect estimates and its extensions to investigate heterogeneity	pg 7,8 & 10	
6 Certainty of evidence	Describe the methods used to assess certainty of the synthesis findings	pg 8	Table S2
7 Data presentation methods	Describe the graphical and tabular methods used to present the effects (e.g., tables, forest plots, harvest plots). Specify key study characteristics (e.g., study design, risk of bias) used to order the studies, in the text and any tables or graphs, clearly referencing the studies included	pg 8 & 10	Table S3
Results			
8 Reporting results	For each comparison and outcome, provide a description of the synthesised findings, and the certainty of the findings. Describe the result in language that is consistent with the question the synthesis addresses, and indicate which studies contribute to the synthesis	pg 8-13	
Discussion			
9 Limitations of the synthesis	Report the limitations of the synthesis methods used and/or the groupings used in the synthesis, and how these affect the conclusions that can be drawn in relation to the original review question	pg 16	

PRISMA=Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
*If the information is not provided in the systematic review, give details of where this information is available (e.g., protocol, other published papers (provide citation details), or website (provide the URL)).